Fall 2013

Neural Encoding of Complex Signals in the Healthy and Impaired Auditory Systems

Saradha Ananthakrishnan
Purdue University

Graduate School ETD Form 9
(Revised 12/07)

PURDUE UNIVERSITY
GRADUATE SCHOOL
Thesis/Dissertation Acceptance

This is to certify that the thesis/dissertation prepared

By Saradha Ananthakrishnan

Entitled

Neural Encoding of Complex Signals in the Healthy and Impaired Auditory Systems

For the degree of Doctor of Philosophy

Is approved by the final examining committee:

Dr. Ananthanarayan Krishnan
Chair

Dr. Christine M. Weber-Fox

Dr. Edward Bartlett

Dr. Xin Luo

To the best of my knowledge and as understood by the student in the *Research Integrity and Copyright Disclaimer (Graduate School Form 20)*, this thesis/dissertation adheres to the provisions of Purdue University's "Policy on Integrity in Research" and the use of copyrighted material.

Approved by Major Professor(s): Dr. Ananthanarayan Krishnan

Approved by: Dr. Keith Kluender 10/03/2013
Head of the Graduate Program Date

NEURAL ENCODING OF COMPLEX SIGNALS IN THE HEALTHY AND IMPAIRED AUDITORY SYSTEMS

A Dissertation

Submitted to the Faculty

of

Purdue University

by

Saradha Ananthakrishnan

In Partial Fulfillment of the

Requirements for the Degree

of

Doctor of Philosophy

December 2013

Purdue University

West Lafayette, Indiana

To Amma and Appa

ACKNOWLEDGEMENTS

Though it is just my name that appears on the cover of this dissertation, the completion of my Ph.D. would not have been possible without the contributions, support and encouragement of several individuals, including my teachers, colleagues, friends and family-members. It is a great pleasure to thank all the people who have made this thesis possible and ensured that my graduate school experience is one that I shall forever cherish.

First and foremost, I would like to express my heartfelt and sincere gratitude to my advisor, Dr. Ravi Krishnan, who has been a great role model and mentor par excellence. He is a stellar research scholar with a vast and in-depth knowledge of auditory evoked potentials. It is under his tutelage and training that I have grown as a researcher, and developed my knowledge and skills in auditory electrophysiology, as well as an ability to think independently. His thorough, patient guidance and unmitigated support were essential in the design, execution and implementation of my research experiments, which more often than not, diverged from the primary research focus of our laboratory. Most importantly, I am deeply thankful for the flexibility he was willing to provide and his constant encouragement as I progressed through the doctoral program. This thesis would not have been possible without his help, and it has truly been an honor and a privilege to work with him.

I would also to offer special thanks to my committee members, Dr. Christine M. Weber-Fox, Dr. Xin Luo and Dr. Edward Bartlett for their support, advice and helpful suggestions. They have been a wonderful group of experts to work with, always available for a discussion and ready to provide insights that stimulated many a new experiment. Thank you all for your guidance and encouragement.

It has been an honor and a privilege to spend the past five years in the Department of Speech, Language and Hearing Sciences at Purdue University, and its members will always remain dear to me. Many senior faculty members helped shape my development during my tenure as a graduate student. In particular, I would like to thank Dr. Jack Gandour, the co-PI in the Auditory Electrophysiology Laboratory. It has indeed been an honor to work with an academic of his caliber. In working with him over the past five years, I have imbibed from him many healthy and useful research habits, including the importance of attention to detail and an understanding of applied statistics. I would also like to extend my sincere gratitude to the Department Chair, Dr. Keith Kluender, who took an enthusiastic interest in my progress and was always supportive and respectful of my endeavors. I would also like to acknowledge and express my thanks to the clinical faculty at Purdue SLHS, who provided me with the rigorous training required to become an efficient audiologist. In addition, I thank all the faculty, staff and students unnamed here who made Purdue SLHS an intellectually stimulating and friendly atmosphere.

I would like to express my gratitude to Purdue University for providing financial support over the entire course of my doctoral program. As a graduate student, I was funded by a Ross Fellowship and a NIH grant (R01-DC008549 grant awarded to Dr. Ravi Krishnan) in conjunction with departmental research and teaching assistantships. I would

also like to thank the past and present Department Chairs, Dr. Robert Novak, Dr. Weber-Fox and Dr. Keith Kluender, for providing financial support for human subject payment and conference-related expenditure through various departmental funds and scholarships.

My dissertation is entirely built on experimental work on human subjects and is a product of more than 150 sessions of data collection. I am much obliged to all the participants who took part in various experiments, and consented to return on multiple occasions for follow-up sessions. I genuinely appreciate the time and energy the participants took out of their everyday schedules to be a part of these experiments.

Interpretation of experimental work involves a significant amount of applied statistics. I must thank The Purdue Statistical Consulting Services (SCS), in particular, Dr. Bruce Craig, Zachary Hass and Han Wang, who patiently provided me with excellent guidance and assistance on various statistical procedures I was often unfamiliar with.

The members of the Auditory Electrophysiology Laboratory, past and present, deserve my sincerest thanks. None of my experiments that constitute this dissertation could have been successfully completed without their assistance and friendship. In particular, I must thank Gavin Bidelman and Christopher Smalt, who provided me with invaluable guidance (and many laughs) as senior lab members. I owe them special thanks for the many hours they have spent teaching me the fundamentals of digital signal processing, data collection, MATLAB coding and data analysis, as well as their valuable input as I shaped the research questions for my dissertation. I would also like to thank Venkat Vijayaraghavan and Jillian Wendel, who have been wonderful colleagues and an immense help, particularly towards the end of my dissertation, providing significant

assistance with data collection, analysis and presentation. It was a pleasure working with all of you!

I could not have survived the roller-coaster journey that is graduate school without the company of the many friends I made at Purdue. These friendships have been a source of laughter, joy and support and extend well beyond our shared adventures in West Lafayette. There are too many names to mention and too little space provided, but I would like to express my warmest thanks to all of them for making my time at Purdue so enjoyable. Many thanks also to all my friends from my undergraduate education in Mumbai. Special thanks to Susmitha C.G., Ranjani Padmanabhan, Shalini Oruganti and Mohan Gopaladesikan—I always smile when I think of all the fun times I have shared with all of you. Thanks for keeping me sane, guys!

Most importantly, I owe my deepest gratitude to my wonderful family; their unwavering love and support are indisputably the bedrock upon which my life has been built. I especially want to thank my parents who have always been an incredible source of unconditional love and constant encouragement. They have lived every up and down of my life with me thus far—mentally, emotionally and physically. They have provided advice, instilled confidence and had faith in me, even in moments when I doubted my own ability. I am the person I am today only because of my parents, and hence it is only fitting that this thesis is dedicated to them—thank you, Amma & Appa. I must also acknowledge my brother and sister-in-law, Ravi and Srividya, who have been wonderful guardians in a country far away from home. They have both always been a great source of support, help, advice and friendship, ensuring that my life as an international graduate student was never lonely or uncomfortable.

Finally, I would like to express my sincerest thanks and warmest gratitude to all of those who supported and helped me in any capacity during the progress and completion of my dissertation. If I have missed thanking anyone, it is a mistake of the mind, not of the heart.

TABLE OF CONTENTS

Page

Page

Page

Page

Page

Page

LIST OF FIGURES

Figure Page

Figure Page

Figure Page

Figure Page

Figure Page

Figure Page

ABSTRACT

Ananthakrishnan, Saradha. Ph.D., Purdue University, December 2013. Neural Encoding of Complex Auditory Signals in the Healthy and Impaired Auditory Systems. Major Professor: Ananthanarayan Krishnan.

Individuals with sensorineural hearing loss (SNHL) typically experience difficulty in understanding speech. Our current knowledge of deficits in speech perception and encoding consequent to SNHL is restricted to psychophysical studies in humans and single-unit experiments in animals. The nature of degradation in neural encoding of speech following hearing impairment in humans has not been extensively researched. The objective of this dissertation is to provide a systematic evaluation of neurobiological signature of hearing loss at the subcortical level using an objective, electrophysiological, non-invasive neural index, the frequency following response (FFR). Subcortical neural encoding of speech signals is explored by quantifying the effects of hearing loss on brainstem processing of acoustic features important for pitch and speech perception, namely the envelope (fundamental frequency or F0) and temporal fine structure (TFS) (formant structure). In order to capture neural encoding of hearing impaired speech perception in various real-world situations, brainstem representations of envelope and TFS cues are studied in response to a variety of stimuli presented in a number of different listening situations.

Subcortical neural representations of envelope and TFS in response to stimuli presented in quiet listening conditions are investigated in the first part of the dissertation. Evidence from the brainstem FFR suggests that neural phase locking of both envelope (F0) as well as TFS (formant related harmonics) is reduced in hearing impaired (HI) subjects as compared to normal hearing (NH) subjects, when stimuli are unadjusted for audibility. The question then emerges if these degraded neural representations of envelope and TFS persist when stimuli are presented at equal audibility. Comparisons of the brainstem FFR at equal audibility levels between NH and HI continue to demonstrate group differences, albeit reduced, suggesting that degradation of the neural representation in hearing loss cannot be attributed wholly to audibility. Rather, these representations appear to reflect a complex interplay of attenuation and distortion effects subsequent to SNHL. Further, envelope and TFS encoding are sensitive to pitch contour and formant structure.

The second part of the dissertation addresses subcortical encoding of envelope and TFS cues following SNHL in degraded listening conditions such as reverberation and background noise. Results indicate a definite degradation of subcortical speech encoding with increased background noise and reverberation in both NH and HI subjects, although these effects are dependent on stimulus, level and type of degradation.

Thirdly, this dissertation examines sources of variation in brainstem speech encoding. Overall, findings suggest that degree of hearing loss, hearing aid satisfaction and music experience may be strong predictors of the fidelity of neural representation of certain acoustic features as reflected in the FFR in hearing impairment.

Finally, the results of this dissertation establish the FFR as a viable technique to measure brainstem speech encoding in hearing impaired listeners to a range of stimuli in a variety of listening conditions. Translation of the brainstem FFR from the lab to the clinic would add great value to the existing audiological test battery, and the potential clinical applications of the FFR are discussed.

CHAPTER 1. OBJECTIVES & ORGANIZATION

1.1 Objectives

Hearing loss is a global issue that affects a staggering 360 million persons worldwide (World Health Organization, 2008; Tucci, Merson & Wilson, 2009). Sensorineural hearing loss occurs when receptor cells in the inner ear are damaged, and is characterized by a loss in sensitivity to sounds and degraded frequency selectivity, which in turn results in difficulty in hearing and understanding speech, particularly in adverse listening conditions. Considerable research efforts have been made to understand the nature of sensorineural hearing loss. Psychophysical (Fitzgibbons & Wightman, 1982; Gagné, 1988; B. Moore & Glasberg, 1988; Bacon & Viemester, 1985) , behavioral (Bacon, Opie, & Montoya, 1998; Baskent, 2006; Buss, Hall, & Grose, 2004; Ching, Dillon, & Byrne, 1998; Dubno & Schaefer, 1992; Duquesnoy & Plomp, 1980; Festen & Plomp, 1990; George & Goverts, 2010; Hopkins & Moore, 2011; Hopkins, Moore, & Stone, 2008; III, Buss, & Grose, 2008; Leek & Summers, 1996; Lorenzi, Debruille, Garnier, Fleuriot, & Moore, 2009; Lorenzi, Gilbert, Carn, Garnier, & Moore, 2006; B. C. J. Moore, 2008; Nábělek & Dagenais, 1986; Nábělek, Ovchinnikov, Czyzewski, & Crowley, 1996; Nábělek & Robinson, 1982; Nábělek, 1988; Nábělek, Letowski, & Tucker, 1989; Smoorenburg, 1992; Summers & Leek, 1998, 1994), and neurophysiologic (M. G. Heinz & Young, 2004; M. Heinz, 2012; Henry & Heinz, 2012, 2013; Henry, Kale,

Scheidt, & Heinz, 2011; Miller, Schilling, Franck, & Young, 1997; Wong, Miller, & Calhoun, 1998; Woolf, Ryan, & Bone, 1981) literature is replete with evidence documenting the differences between normal hearing and hearing impaired systems with respect to neural encoding and perception of pitch and speech. While decades of research have established a clear effect of hearing impairment on speech perception, several aspects of hearing impairment continue to baffle researchers, clinicians and patients alike. For instance, why do two listeners with the same degree and configuration of hearing loss have differences in benefit from amplification, or speech perception abilities? Also, what accounts for similar patterns of benefit from amplification or identical speech perception scores in two individuals who exhibit different audiological profiles? In order to gain a better understanding of the effects of hearing impairment, it is important that perceptual deficits in hearing impairment are related to their underlying neural representations. While there has been a renewed interest in evaluating the nature of degradation in neural encoding of acoustic features important for pitch and speech perception in hearing impaired individuals, existing research literature in humans to date is rather sparse (Plyler & Ananthanarayan, 2001; Anderson, Parbery-Clark, White-Schwoch, Drehobl & Kraus, 2013).

Given this large gap in research on the neural bases of hearing-impairment in humans, the objective here is to provide a systematic evaluation of neurobiological signature of hearing loss at the subcortical level, by characterizing and quantifying the effects of hearing impairment on brainstem pitch and speech encoding using the Frequency Following Response (FFR). The FFR is a scalp recorded evoked potential that reflects neural activity in an ensemble of neural elements, synchronized to the individual

cycles of the stimulus waveform (phase-locking). Results from a series of five experiments are presented in this dissertation, in an effort to delineate the nature of degradation of neural representation of steady state and time variant complex sounds in hearing-impaired individuals in quiet and adverse listening conditions. Also, the results of these experiments may facilitate development of optimal signal processing strategies for recovering degraded neural representation.

1.2 Organization

Chapter 2 reviews the literature on the frequency following response, laying the foundation for this subcortical electrophysiologic measure of neural encoding of complex sounds as a plausible technique to study hearing impairment. Findings from the few studies that have used the FFR to analyze speech encoding in hearing impairment are summarized, setting up a strong framework for Experiments 1-5 in the dissertation.

Chapter 3 provides a comprehensive look at the general methods used in all the experiments conducted as part of this dissertation.

Chapter 4 reports on FFR degradation consequent to mild-moderate sensorineural hearing impairment with respect to specific neural features of a signal (the envelope and temporal fine structure (TFS)) when presented with a steady state vowel. Using the steady state vowel allowed for group differences to be indexed first in response a stimulus with a relatively "simple pitch" (steady state) that was also ecologically relevant (speech), laying the foundation for subsequent experiments. A closer analysis of the hearing impaired performance in Chapter 4 indicates a subset of high performing hearing impaired subjects; their audiological and demographical profiles are examined in detail.

Overall, findings suggest that degree of hearing loss, hearing aid satisfaction and music experience may be strong predictors of the fidelity of neural representation of certain acoustic features as reflected in the FFR in hearing impairment.

As a logical follow-up to findings from Chapter 4, Chapter 5 addresses the role of audibility in the normal and impaired auditory systems. Comparisons at equal audibility levels between normal hearing and hearing impaired continue to demonstrate group differences, albeit reduced; suggesting that degradation of the neural representation in hearing loss cannot be attributed wholly to audibility.

The steady state vowel stimulus used in Chapters 4 and 5, while ecologically relevant, was a "simple" stimulus in terms of a speech sound, whereas real-world speech is typically more complex and dynamic. Chapter 6 examines the role of stimulus complexity and hearing acuity on the neural representation of different acoustic features, and demonstrates a degradation of neural encoding of envelope and TFS encoding as a function of stimulus complexity and context. Hearing loss related differences are preserved for all stimuli for envelope encoding; similar effects are observed for TFS encoding for steady-state and time varying speech stimuli, but not for the non-speech stimulus.

Behavioral and neurophysiologic animal studies have shown a degradation of neural encoding of speech sounds in challenging listening situations. Chapters 7 and 8 address the effects of degraded listening conditions (noise and reverberation) on neural encoding in the normal hearing and hearing impaired listeners. Overall results indicate a definite degradation of subcortical speech encoding with increased background noise and reverberation in both normal hearing and hearing impaired listeners, although these

effects are dependent on stimulus and level of degradation. The effects of adverse listening conditions on neural representation of speech sounds also vary with the type of degradation applied. While neural encoding of both envelope and TFS cues appear to be degraded with background noise, reverberation induced changes are more significant for neural encoding of TFS than envelope.

In Chapter 9, the possible sources of variation contributing towards neural encoding of speech as indexed by the FFR are analyzed. Audiometric indices of hearing loss and hearing aid use and satisfaction emerge as factors that could shape the neural encoding of speech sounds in the hearing impaired system.

Finally, Chapter 10 summarizes the findings from Chapters 1-9 to draw overall conclusions with respect to the effect of hearing impairment on subcortical speech encoding. The end goal through any research involving hearing impairment is translation to clinical applicability, and the relevance of findings from this dissertation are discussed in the context of clinical audiology.

CHAPTER 2. LITERATURE REVIEW

2.1 Speech perception and encoding in hearing loss

Degraded encoding and perception of speech sounds in sensorineural hearing impairment has been documented by numerous psychophysical (Fitzgibbons & Wightman, 1982; Gagné, 1988; B. Moore & Glasberg, 1988; Bacon & Viemester, 1985), behavioral (Bacon et al., 1998; Baskent, 2006; Buss et al., 2004; Ching et al.,1998; Dubno & Schaefer, 1992; Duquesnoy & Plomp, 1980; Festen & Plomp, 1990; George & Goverts, 2010; Hopkins & Moore, 2011; Hopkins et al., 2008; Buss, & Grose, 2008; Leek & Summers, 1996; Lorenzi et al., 2009; Lorenzi et al., 2006; B. C. J. Moore, 2008; Nábělek & Dagenais, 1986; Nábělek et al., 1996; Nábělek & Robinson, 1982; Nábělek, 1988; Nábělek et al., 1989; Smoorenburg, 1992; Summers & Leek, 1998, 1994) and neurophysiologic experiments (M. G. Heinz & Young, 2004; M. Heinz, 2012; Henry & Heinz, 2012, 2013; Henry et al., 2011; Miller et al., 1997; Wong et al., 1998; Woolf et al., 1981) . While a majority of experiments demonstrate an exacerbation in hearing impaired speech encoding and perception in challenging listening conditions such as background noise or reverberation (Duquesnoy & Plomp, 1980; Festen & Plomp, 1990; Frisina & Frisina, 1997; Gardi & Merzenich, 1979; Henry & Heinz, 2012; Leek & Summers, 1996; Nábělek & Dagenais, 1986; Nábělek, 1988; Smoorenburg, 1992) there are several behavioral and animal physiology studies that have demonstrated that differences

between normal hearing and hearing impaired listeners in speech perception and encoding are also present in quiet listening conditions (Miller et al., 1997; Nábělek, 1988; Summers & Leek, 1998; Woolf et al., 1981).

Reviewed here is the literature on speech perception and encoding in sensorineural hearing loss (SNHL), which is largely dominated by behavioral studies in humans and neurophysiologic data in animals. Also reviewed is the human frequency following response, which is an objective index of neural phase-locking, and the few studies that have used the FFR to examine the neural mechanisms of speech encoding in hearing impairment.

2.2 Effect of hearing loss

2.2.1 Evidence from psychophysical studies

Psychophysical literature is replete with studies documenting weaker pitch perception in hearing impaired listeners as compared to normal hearing listeners. Frequency difference limen (FDL) experiments in listeners with normal hearing and cochlear hearing loss have found a significant effect of hearing impairment on frequency discrimination (Gengel, 1973; Tyler, Wood & Fernandes, 1983; Hall & Wood; 1984, Freyman & Nelson, 1986; 1987;1991, Moore & Glasberg, 1986; Moore, Peters & Glasberg, 1992; Simon & Yund, 1993). Moore et al. (1992) found greater FDLs in young and old listeners with cochlear hearing loss as compared to young normal hearing listeners. Frequency modulation difference limens measured in listeners with SNHL increased as a function of hearing loss, with a greater effect at low frequencies as compared to high frequencies (Zurek & Formby, 1981). Moore and Glasberg (1986)

measured FMDLs in hearing impaired listeners at 80 dB SPL for a low frequency (500 Hz) and a high frequency (1000 Hz). FMDLs were larger in hearing impairment, with a differential frequency effect where low frequencies were affected to a greater extent than high frequencies. FMDLs were found to consistently be up to 9.5 times larger in listeners with cochlear hearing loss even when stimuli were presented at comfortable listening levels for the hearing impaired listeners (Grant, 1987).

2.2.2 Evidence from speech perception studies

Numerous behavioral studies have examined the effects of hearing impairment on perception of speech and speech-like signals. Leek and Summers (1996) investigated perception of vowel like sounds in normal hearing individuals in quiet and in a simulated moderate hearing loss condition (using broad-band noise). Spectral contrast measurements between peaks and valleys of vowel formants indicated that greater amount of spectral contrast was required in the simulated moderate hearing loss condition.

Nábělek (1988) found a strong correlation between audiometric threshold and vowel identification in hearing impairment, but not between age and vowel identification.

Summers and Leek (1994) examined F0 discrimination for steady state vowels (including /u/, used in the current experiment) with F0s ranging from 120-150 Hz in normal hearing and hearing impaired listeners. Correlation analyses of F0DL with different audiometric thresholds indicated that high frequency regions play a key role in F0 discrimination in hearing impaired listeners as opposed to low frequency regions in normal hearing.

2.2.3 Evidence from cortical potentials

Oates, Kurtzberg, & Stapells (2002) examined cortical event related potentials supplemented by behavioral measures in normal hearing and hearing impaired individuals in response to speech sounds. Specifically, they studied the effect of hearing loss on the response parameters (i.e. amplitude and latency) of the N1, MMN, N2 and P3 evoked response potentials (ERPs) in response to /ba/ and /da/ presented in an oddball paradigm at two intensity levels (65 and 80 dB SPL). The hearing impaired participants ranged from mild to severe to profound losses and the mean ages of the subjects in both groups were closely matched. Results from the study indicate that ERP latencies were delayed in the hearing impaired group, even for participants with mild hearing loss. Latency was found to be more sensitive than amplitude to effects of hearing loss, with amplitude reductions noted only when average thresholds (at 1000 and 2000 Hz) were greater than 60 dB HL. Further, it was observed that late ERPs demonstrated a greater change in response parameters with hearing loss as compared to earlier ERPs such as the N1 and MMN. Per Oates et al., (2002), this result indicates that SNHL has stronger effects at higher cortical levels than at lower cortical levels which reflect more sensory, pre-attentive signal processing.

2.2.4 Evidence from neurophysiologic studies

Woolf et al. (1981) examined neural phase locking in response to low frequency pure tones at the level of the auditory nerve and cochlear nucleus in chinchillas with normal hearing and ototoxicity induced outer hair cell destruction (preserving normal inner hair cell function). Findings from this study indicated that neural synchrony was

disrupted in a frequency dependent pattern consistent with audiometric thresholds. The differences in neural phase locking persisted at higher sensation levels where audibility was eliminated as a contributing factor. However, these findings are not in agreement with results from Harrison and Evans (1979), which did not show a decrease in neural phase locking with kanamycin induced OHC damage in chinchillas in response to pure tones. Similarly, Miller et al. (1997) demonstrated no significant differences in phase locking to pure tones in cats with noise induced hearing loss (NIHL). Phase locking to pure tones was only mildly affected in chinchillas with SNHL (Henry & Heinz, 2012).

Neural synchrony in response to broadband signals, on the other hand, consistently shows degradation with hearing loss. Miller et al., (1997) and Wong et al., (1998) analyzed auditory nerve single unit data in response to a steady state vowel in normal hearing cats and cats with noise induced hearing loss. The vowel /e/ had a fundamental frequency at 100 Hz and formants at 500 Hz, 1.7 kHz and 2.5 kHz. Robust phase-locking was observed in normal hearing animals at the fundamental as well as formant frequencies; recall that phase-locking at the level of the AN extends up to 5 kHz. Phase-locking in cats with NIHL occurred at a broad range of frequencies not limited to the fundamental or formant frequencies, resulting in a “diffuse” and “broad-band” pattern (Miller et al., 1997; J. Wong et al., 1998).

2.2.5 Neural plasticity effects

Neural plasticity in the auditory system refers to a variety of physiological/anatomical changes can take place in the neuronal units of the brain and brainstem subsequent to hearing loss, causing a reorganization of the neurons in auditory

system. Plasticity effects may be related to hearing loss (reduced auditory input due to signal attenuation and distortion in hearing loss), as well as effects arising from the use of amplification (Willott, 1996). Neural plasticity can occur at all levels in the auditory system; hearing loss induced plasticity effects have been documented in animal studies (Syka, 2002; Willott, 1996) at cortical as well as subcortical levels. At the neuronal level, these plastic changes may cause axonal sprouting from healthy to damaged regions, establishing new neural circuits, or alter existing neural circuits by a loss of inhibition mechanisms. Plastic changes caused by reduced auditory input may cause rewiring of tonotopic maps due to hair cell damage, reorganization of spatial maps that determine directional hearing and hearing in noise and changes in synaptic activity patterns.

2.2.6 Interim summary

The literature reviewed thus far summarizes the effects of hearing impairment on speech encoding and perception described by behavioral and cortical evoked potential studies in humans and neurophysiologic data in animal models. However, the neural encoding of speech sounds in humans with hearing impairment remains largely uninvestigated. The frequency following response, an objective index of neural phase-locking at the brainstem level, may provide answers to bridge the gap between data from behavioral studies and animal neurophysiology and is reviewed next.

2.3 The Frequency Following Response (FFR)

The primary analysis tool employed in the experiments described in this dissertation is the frequency following response. Presented in this chapter is a thorough

literature review describing this subcortical electrophysiological response, research applications of the FFR in various populations and FFRs in hearing impairment.

2.3.1 What is the FFR?

The scalp-recorded human frequency following response (FFR) was first described by Moushegian, Rupert, & Stillman in 1973. The hallmark of the FFR is its ability to mimic the stimulus waveform through sustained neural phase-locked activity at the level of the rostral brainstem (Glaser, Suter, Dasheiff, & Goldberg, 1976; Smith, Marsh, & Brown, 1975). The exact anatomical generator of the FFR remains a matter of debate and various sites have been implicated: the inferior colliculus (Smith et al., 1975), cochlear nucleus and superior olivary complex (Gardi, Merzenich & McKean, 1979), auditory nerve (Snyder & Schreiner, 1984). Collectively, these different experiments seem to suggest that several major auditory nuclei may play a role in the generation of the FFR. The FFR occurs at a latency of about 6 ms (Daly, Roeser, & Moushegian, 1976; Gerken, Moushegian, Stillman, & Rupert, 1975; Glaser et al., 1976; Marsh, Brown, & Smith, 1974; Moushegian et al., 1973; Smith et al., 1975) which corresponds to an upper brainstem origin. Smith et al. (1975) demonstrated strong evidence towards the IC as the site of origin for the FFR by comparing FFR latencies through scalp recordings and direct recordings from auditory nuclei in cats. In addition, cooling of the IC reduced the FFR whereas the SOC did not demonstrate such an effect. As the spectra as well as upper frequency limits of the FFR are similar in cats and humans (Greenberg, Marsh, Brown, & Smith, 1987), one may extrapolate that the inferior colliculus is also the site of origin for the FFR in humans. Various experiments (Galbraith et al., 2000; Smith et al., 1975;

Stillman, Crow, & Moushegian, 1978) have suggested that the relatively longer latency (about 6-8 ms) of FFRs recorded with a vertical electrode montage suggests an origin in the rostral brainstem while the shorter latency (2-3 ms) response recorded using a horizontal electrode montage indicates a more peripheral (acoustic nerve) origin. The FFR demonstrates phase-locking to frequencies between 70-1500 Hz (Gardi & Merzenich, 1979; Glaser et al., 1976; Stillman et al., 1978; Starr & Hellerstein, 1971) with the largest response amplitude at or below 500 Hz (Moushegian et al., 1973; Marsh et al., 1975; Smith et al., 1975; Veld, Osterhammel, & Terkildsen, 1977). The FFR is typically recorded 30-60 dB above the behavioral threshold (Moushegian et al., 1973; Davis & Hirsh, 1976). No differences were observed in monaural vs. binaural FFR recordings indicating that two independent neural sources are responsible for generating the FFR, for the right and left auditory pathways (Gerken et al., 1975).

2.3.2 Neural encoding of complex sounds using the FFR

Through its unique ability of phase-locking, the FFR provides an objective, non-invasive window to study neural encoding of both pitch relevant information and spectra of complex sounds in human as well as animal models. The FFR has been shown to reflect brainstem level neural phase locking to numerous stimuli, such as complex tones with missing fundamentals (Greenberg, Marsh, Brown, & Smith, 1987; Hall, 1979), two component tones (Greenberg & Marsh, 1979) and inharmonic tones (Chambers, 1986). More recently, the FFR has been recorded to the first and second formants (F1 and F2) of two tone approximations of steady state vowels (Krishnan, 1999), time varying tonal sweeps (Krishnan & Parkinson, 2000), for time varying complex speech sounds such as

formant transitions (Plyler & Ananthanarayan, 2001), Mandarin tones and iterated rippled noise (IRN) (Krishnan, Xu, Gandour, & Cariani, 2004, 2005; Krishnan & Gandour, 2009; Xu, Krishnan & Gandour, 2006; Song, Skoe, Wong, & Kraus, 2008; P. Wong, Skoe, & Russo, 2007), musical intervals, consonant-vowel stimuli (Banai et al., 2009; Cunningham, Nicol, & Zecker, 2001; King, Warrier, Hayes, & Kraus, 2002; Musacchia, Sams, Skoe, & Kraus, 2007; Nicole Russo, Nicol, Musacchia, & Kraus, 2004; Wible, Nicol, & Kraus, 2004, 2005). Further, the FFR has also been recorded in degraded listening conditions such as reverberation (Bidelman & Krishnan, 2010) and noise (Cunningham et al., 2001, Russo et al., 2004, Russo et al., 2005, Russo et al., 2008).

The FFR has been used to demonstrate differences in neural encoding of envelope and TFS related cues in populations with different clinical conditions. The FFR has been shown to have a degraded representation of TFS cues relative to envelope cues in individuals with language based learning problems (Banai et al., 2009; Banai, Nicol, Zecker, & Kraus, 2005; Cunningham et al., 2001; King et al., 2002; Wible et al., 2004) and the reverse in autism spectrum disorders (N Russo, Nicol, & Trommer, 2009).

Subcortical studies evaluating representation of pitch-relevant information have shown that neural encoding of pitch is strongly shaped by experience dependent learning effects. Krishnan, Gandour, & Bidelman (2012) provide an excellent review of subcortical studies investigating neural plasticity with respect to language and music. Pitch representation of time varying stimuli (e.g. Mandarin tones) native to speakers of tonal languages (e.g. Chinese) has been found to be more robust in tone-language speakers (Chinese speakers) as compared to speakers of non-tonal languages (e.g. English); these differences persist when the stimulus is degraded. Similar to differences

in subcortical encoding in different language groups, FFRs are more robust in musicians as compared to non-musicians when a musically relevant signal is presented. Interestingly, cross domain studies of music and language indicate that experience dependent effects are not specific to a particular domain but are transferrable across areas. The sensitivity of the FFR to experience dependent learning effects has potential clinical implications with respect to indexing benefits from "secondary plasticity" which may be seen in consequent to amplification or auditory training.

2.3.3 Neural encoding of different acoustic components using the FFR

The frequency following response to speech is a harmonically rich response, representing brainstem encoding to several defining acoustic features of the incoming signal. Kraus and Nicol (2005) extended the source-filter theory of speech production to explain speech encoding by the FFR; specifically, the FFR is capable of phase-locking to the fundamental frequency (F0) (representing "source" information) as well as higher F0-related harmonics, some of which are enhanced depending on the stimulus formant structure ("filter" information). Source information is encoded by the periodicity of the FFR; in other words, the reciprocal of the time interval between the FFR peaks is equal to the stimulus F0. Superimposed on the periodicity of the FFR are higher frequency fluctuations which represent the "filter" characteristics or encoding of formant related information.

The FFR reflects the frequency of the stimulus envelope ("envelope FFR") as well as the spectral structure ("spectral FFR") of the stimulus (Aiken & Picton, 2008; Krishnan, 2007). As FFR_{ENV} is unaffected by stimulus polarity (Krishnan, 2002; Small &

Stapells, 2005), it becomes possible to tease apart the neural encoding of envelope and spectral cues, using additive and subtractive techniques. The ability of the FFR to encode fundamental frequency cues has been repeatedly demonstrated (Bidelman, Gandour, & Krishnan, 2011; Krishnan et al., 2004; Krishnan, 2002; Smalt, Krishnan, Bidelman, Ananthakrishnan, & Gandour, 2012; Swaminathan, Krishnan, & Gandour, 2008; Xu et al., 2006). While significant information about brainstem level pitch encoding can be gleaned from the fundamental frequency (F0) encoding strength in the FFR in various populations, this measure is not reflective of place specific encoding of signals on the basilar membrane. As discussed by Aiken and Picton (2008), the fundamental frequency represents the envelope modulation frequency for the speech signal, which may be decoded via speech information at any frequency; hence F0 of a speech signal need not be encoded in a place-specific manner on the basilar membrane. Spectral FFR measures, on the other hand, reflect brainstem encoding of the harmonic structure of the incoming speech signal, which is encoded in a place specific manner. It becomes especially important to measure both envelope and spectral FFRs when discussing brainstem speech encoding in hearing impairment, where there could be a place specific impairment of receptor cells on the basilar membrane i.e. a differential effect of hearing loss across frequency.

2.3.4 Derivation of envelope and spectral FFR

Adding FFRs collected in opposite polarities yields an FFR dominated by neural phase locking to the stimulus envelope with little or no phase locking to the TFS, while subtraction yields the spectral FFR (Aiken & Picton, 2008; Krishnan, 2002). Extraction

of neural phase locking to the spectral components of the stimulus by subtracting responses in opposite polarities is based on half-wave rectification that occurs during inner hair cell transduction (Brugge, Anderson, Hind & Rose, 1969). According to Brugge et al., (1969), auditory nerve discharges occur maximally during rarefaction polarity. When the stimulus is inverted, discharges occurring at rarefaction polarities in the inverted stimulus correspond in time to the condensation polarity of the original stimulus. Rectification related distortion is removed and stimulus waveform related neural activity is preserved when the compound histograms of these opposite polarities are subtracted ("compound histogram technique"). Translation of results from the compound histogram technique to the brainstem FFR is acceptable as both techniques are indices of neural synchrony. Based on this assumption, it is reasonable to extend Brugge's findings to the brainstem FFR and infer that subtracting opposite polarity FFRs eliminates the half-wave rectification related distortions, while preserving the stimulus waveform related neural encoding. In this case, the rectification related distortions reflect the envelope FFR.

Aiken and Picton (2008) provide a theoretical model to explain the additive and subtractive processes that give rise to the envelope and spectral FFR. As polarity inversion effects are not significant for envelope modulation, no differences are noted when FFRs in opposite polarities are summed; envelope locking is preserved. On the other hand, subtracting responses in opposite polarities eliminates the envelope FFR, leaving behind only the spectral FFR.

2.3.5 FFR & hearing loss

While the FFR has been applied as a useful tool to analyze various populations, there are only a handful of studies addressing the effects of hearing impairment on the FFR.

Yamada, Yamane & Kodera (1977) investigated whether the FFR can be recorded in hearing impaired subjects, its possible origins and correlations between the FFR and ABR. The hearing impaired participants in this study comprised of individuals with varying audiometric configurations (flat vs. high frequency hearing loss) and included different types of hearing loss (conductive and sensorineural). Yamada et al., (1977) simultaneously recorded FFRs and ABRs evoked by a low frequency tone burst at multiple intensity levels in normal hearing and hearing impaired participants. They found that the FFR could be recorded as low as 30-40 dB HL in normal hearing participants. FFRs were also present at levels corresponding to normal hearing listeners in all participants with severe high frequency hearing loss and normal audiometric thresholds at 500 Hz. As the ABR and FFR could be elicited even in individuals with high frequency hearing loss, Yamada et al., (1977) suggest that both the FFR and the ABR may be initiated before the basal turn of the cochlea, in the apical or middle turns, contrary to findings from Davis & Hirsch (1976) which support a basal origin for these responses. FFR-ABR thresholds differed by 20-30 dB difference in normal hearing/conductive hearing loss. Whereas, a strong FFR-ABR correspondence (within 10 dB) was noted in subjects with flat sensorineural hearing loss, possibly due to loudness recruitment in SNHL.

Daly et al., (1976) collected FFRs in participants with normal hearing and profound unilateral sensorineural hearing loss with the objective of studying binaural interaction effects and FFR sources. Stimuli were 500 Hz tone bursts presented at 50 dB SL for both groups, which were also age-matched. In the normal hearing subjects, ipsilateral stimulation was always greater than contralateral stimulation. Binaural stimulation yielded larger responses than monaural stimulation of either ear. The sum of the monaural ipsilateral responses was greater than the binaural response. In the hearing impaired subjects, monaural stimulation of the unimpaired ear yielded an FFR, but no response was obtained when the impaired ear was stimulated. In addition, FFRs from binaural stimulation were similar to FFRs obtained from monaural stimulation of the unimpaired ear. Extending binaural interaction effect results in normal hearing subjects, the authors also discuss the possibility that the FFR originates from two different neural generators; the FFR origin may be different from the generators responsible for the ABR or reflect iterative responses from ABR generators, or include both these mechanisms. As the main focus of this article was centered on binaural vs. monaural effects on the FFR, no comparisons were reported between the normal hearing and hearing impaired group.

Overall these results indicate that the FFR can indeed be recorded in individuals with sensorineural hearing loss, keeping in mind type, audiometric configurations and degree of hearing loss. It is reasonable to extend findings from Yamada et al., (1977) and Daly et al., (1976) to suggest that FFRs may be recorded in flat and sloping sensorineural hearing loss not exceeding a severe degree.

While the above FFR studies included individuals with sensorineural hearing impairment, the primary questions of interest in these two experiments were not related to

effects of hearing loss on brainstem neural phase-locking. To date, there are only two studies in human FFR literature that specifically address the question of subcortical speech representations in sensorineural hearing loss.

The first of these studies is by Plyler and Ananthanarayan (2001), which examines the effect of mild-moderate SNHL on phase-locking ability of the FFR to formant transitions, and compared FFR results to a behavioral identification task. This experiment is reviewed in detail in Chapter 4, as part of the literature review for Experiment 1. Briefly, results indicated that there was a significant reduction in neural encoding as reflected by the ability of the FFR to follow spectral peaks during formant transition. Also of interest is the finding that the effect of hearing impairment on the FFR was reflected in the behavioral results, with decreased performance in the identification task for the hearing impaired group across all stimulus levels. Further, Plyler and Ananthanarayan (2001) also demonstrated that there was no statistical improvement in neural encoding with increases in presentation level in the hearing impaired group suggesting that factors aside from reduced audibility cause degraded FFRs in hearing impairment. The authors point to degraded neural phase locking consequent to broader than normal auditory filters in the hearing impaired system.

Anderson, Parbery-Clark, White-Schwoch, Drehobl & Kraus (2013) investigated the effects of hearing loss on the subcortical representations of speech cues in greater detail, separating differences in envelope and temporal fine structure coding in normal hearing and hearing impaired individuals. Again, this experiment is reviewed in detail in Chapter 4. There has been a significant amount of interest in understanding the differential roles of envelope and TFS cues in sensorineural hearing impairment. In an

attempt to translate findings from behavioral and animal models to the FFR, Anderson et al (2013) found enhanced envelope encoding for the hearing impaired in quiet but not in noise; no differences in TFS encoding were noted in quiet or noise. Per the authors, enhanced envelope in hearing impairment may occur consequent to hearing loss related alterations in excitatory-inhibitory balances. The lack of differences in absolute TFS encoding of normal hearing and hearing impaired individuals found in this study is inconsistent with perceptual, neurophysiological and modeling literature. Anderson et al acknowledge this, and indicate the need for testing TFS differences at multiple sound presentation levels and signal to noise ratios, which may yield group differences.

2.4 Conclusion

Put together, findings from Plyler and Ananthanarayan (2001) and Anderson et al., (2013) suggest that inability in hearing impairment to faithfully follow the frequency change present in formant transitions, with differential encoding of temporal speech cues, namely the neural envelope and TFS. These experiments are pioneering pieces of work with respect to brainstem speech encoding in hearing impairment. However, many unanswered questions remain in our understanding of the consequences of SNHL on the neural representation of speech sounds. Are effects of hearing impairment on the FFR affected by stimulus complexity? How does the nature of neural encoding of complex sounds vary within a group of hearing impaired subjects? Can the neural encoding of speech as indexed by the FFR be predicted by a statistical model incorporating various subject related factors? How does neural representation of complex stimuli compare between normal hearing and hearing impaired FFRs when audibility is accounted for? Do

challenging listening conditions degrade neural indices of speech encoding in hearing impaired individuals, and if so, is the pattern of degradation similar to that in the normal hearing FFR? How do FFR measures in normal hearing and hearing impaired group compare to clinical speech perception tests used in audiometric testing? The goal of this dissertation is to answer these questions by providing a systematic evaluation of subcortical encoding of various auditory signals in the normal and impaired auditory system.

CHAPTER 3. GENERAL METHODS

The general methodological procedure used in each experiment described in this dissertation is similar with respect to participant details (demographic information, audiological profiles and case history) and FFR data collection and analysis protocols. Methodology that is common to all five experiments is summarized in this chapter. Any methodological details unique to an experiment are elaborated within the chapter describing that particular experiment.

3.1 Participants

A total of forty-four adult subjects, including twenty-five normal hearing and nineteen hearing impaired subjects with mild to moderate sensorineural hearing loss participated in the FFR experiments. All participants were paid and gave informed consent in compliance with a protocol approved by the Institutional Review Board of Purdue University. Participant details for each experiment are listed below:

3.2 Audiometry

Pure tone audiometry was conducted on all participants as a first step to establish candidacy for the experiment. Air conduction and bone conduction thresholds were obtained at octave frequencies between 250 and 8000 Hz. Immittance audiometry was

performed on each participant to ensure no middle ear pathology was involved. Individuals with air and bone conduction thresholds better than 25 dB HL across the audiometric test frequencies were classified as normal hearing. All hearing impaired participants had mild to moderately-severe (26-70 dB HL) sensorineural hearing loss with varying audiometric configurations.

3.3 Case History

All hearing impaired participants completed an extensive case history, providing demographic details, audiological & medical history and life-style information. See appendix for case history questionnaire.

3.4 Stimuli

Stimulus complexity and listening condition were varied across the experiments. Presented here is a brief summary:

- Experiment 1(Chapter 4): Synthetic steady state English back vowel /u/ [F0=120 Hz; F1=360 Hz; F2=970 Hz] presented in quiet at 80 dB SPL.
- Experiment 2 (Chapter 5): Synthetic steady state English back vowel /u/ [F0=120 Hz; F1=360 Hz; F2=970 Hz] presented in quiet at multiple presentation levels ranging from 60-85 dB SPL in normal hearing and 70-95 dB SPL in hearing impaired participants.
- Experiment 3 (Chapter 6): The following stimuli were all presented in quiet at 80 dB SPL.
    - Complex tone [F0=110 Hz, 15 equal amplitude harmonics]

  - Synthetic steady state English back vowel /u/ [F0=120 Hz; F1=360 Hz; F2=970 Hz]
  - Time-varying (falling) diphthong /au/ [F0=120-114 Hz; F1=680-440 Hz]
- Experiment 4 (Chapter 7): The following stimuli were presented at 80 dB SPL at three different SNRs ("clean", +5 dB and -5 dB)
  - Synthetic steady state English back vowel /u/ [F0=120 Hz; F1=360 Hz; F2=970 Hz]
  - Time-varying (falling) diphthong /au/ [F0=120-114 Hz; F1=680-440 Hz]
- Experiment 5 (Chapter 8): Time-varying (falling) diphthong /au/ [F0=120-114 Hz; F1=680-440 Hz] presented at 80 dB SPL at four different reverberation levels (dry, mild, moderate and severe)

3.5 FFR Data Acquisition

FFR recording protocol and data analysis were similar to those described in Bidelman, Gandour, & Krishnan (2011), Krishnan, Swaminathan, & Gandour (2009), Krishnan, Gandour, Ananthakrishnan, Bidelman, & Smalt (2011). Participants were situated in a comfortable recliner in an acoustically and electrically shielded booth. They were instructed to relax and refrain from extraneous body movements to minimize movement artifacts and ignore the sounds they heard. Subjects were allowed to sleep through the duration of the FFR experiment. FFRs were recorded from each participant in response to monaural stimulation at a fixed sound pressure level (80 dB SPL) at a repetition rate of 2.76/s. The presentation order of the stimuli was be randomized both

within and across participants. The experimental protocol was controlled using a signal generation and data acquisition system (Intelligent Hearing Systems) using a sampling rate of 40 kHz. The stimulus files were routed through a digital to analog module and presented through a magnetically shielded insert earphone (Etymotic, ER-3A). The stimuli were presented in the right ear in normal hearing participants and in the ear with mild-moderate sensorineural hearing loss in the participants with hearing loss.

FFRs were recorded differentially between a non-inverting (positive) electrode placed on the midline of the forehead at the hairline (Fz) and inverting (reference) electrodes placed on (i) the right mastoid (A2) and the left mastoid (A1) linked together; and (ii) the 7^{th} cervical vertebra (C7). Another electrode placed on the mid-forehead (Fpz) served as the common ground. FFRs were recorded simultaneously from the two different electrode configurations, and subsequently averaged for each stimulus condition to yield a response with a higher signal-to-noise ratio (Krishnan et al., 2009). All inter-electrode impedances were maintained below 1 kΩ. The EEG inputs were amplified by 200,000 and band-pass filtered from 50 to 3000 Hz (6 dB/octave roll-off, RC response characteristics). Each response waveform represented the average of 4000 stimulus presentations over a 250 ms (for the steady state stimulus) and 180 ms (for the time varying stimulus) analysis window. The experimental protocol took approximately 120 minutes to complete.

FFRs were recorded to both condensation and rarefaction onset polarities to extract phase-locked neural response to stimulus envelope and temporal fine structure. While addition of the FFRs to these two polarities yield FFRs primarily phase-locked to the envelope of the stimulus (FFR_{ENV}), subtraction of these responses yield FFRs phase-

locked to the fine structure of the stimulus (FFR_{SPEC}) (Aiken & Picton, 2008; Krishnan 2002). Krishnan (2002) found robust peaks at stimulus harmonics, but not at the fundamental (stimulus envelope) when condensation and rarefaction FFRs were subtracted. Adding condensation and rarefaction FFRs removes the cochlear microphonic, stimulus artifact as well as the fine structure information, while preserving the envelope FFR (Small & Stapells, 2005)

3.6 FFR Data Analysis

3.6.1 Temporal Analysis

Autocorrelation analysis was used to estimate the neural pitch period in the FFRs (Krishnan, Gandour, Bidelman, & Swaminathan, 2009, Krishnan et al., 2009; Swaminathan, Krishnan, & Gandour, 2008). In this analysis, the normalized autocorrelation function (expressed as a value between 0 and 1, where 0 corresponds to no periodicity and 1 to maximal periodicity) was computed over the duration of the response (Krishnan et al., 2010). A response peak was selected between 0 and 1 which corresponded to the same location (time lag) of the autocorrelation peak in the input stimulus (Krishnan et al., 2009; Krishnan et al., 2009; Swaminathan et al., 2008). The reciprocal of this time lag (or pitch period) represents an estimate of the f0. The analysis was performed on both the stimuli and the FFR signals to yield estimates of pitch periodicity for both stimulus and response.

Autocorrelograms (ACGs), which are three dimensional plots indexing changes in periodicity and pitch strength as a function of time (Krishnan et al., 2009; Swaminathan et al., 2008), were used to visualize the FFR data. The ACG is structured such that the

horizontal axis represents time and the vertical axis represents the time lags corresponding to the peaks of the autocorrelation function (pitch periods). The intensity of each point in the image reflects the magnitude of the ACF at that particular time lag and time instant.

3.6.2 Spectral Analysis

The FFR spectrum is complex, consisting of spectral peaks at the fundamental frequency (F0) as well as harmonic components, integer multiples of the F0. The Fast Fourier Transform (FFT) analysis can be used to decompose the complex FFR into its component sine waves, the magnitudes of which determine the energy at that particular frequency in the FFR spectrum. Individual frequency spectra were computed per subject per condition over the duration of each FFR by taking the Fast Fourier Transform (FFT) of the FFR waveform. Applying FFT to the addition of condensation and rarefaction FFRs (FFR_{ENV}) yields a response spectrum with peaks at F0 and its multiples. When the FFT is applied to the subtraction of the condensation and rarefaction polarities (FFR_{SPEC}), the response spectrum has robust peaks at stimulus harmonics, particularly at formant related harmonics. Absolute magnitudes (FFTMag) as well as magnitudes relative to the noise floor (FFTMag/Noise Floor and FFTMag-Noise Floor) were measured at the F0 in the FFR_{ENV} condition and formant related harmonics in the FFR_{SPEC} condition. Measurements relative to the noise floor (NF) were used in order to ignore artificial boosts in peak magnitudes due to varying noise floors in each subject. Analysis of variance testing revealed no significant differences in the noise floor for normal hearing and hearing impaired subjects at any of the FFT peaks measured when stimuli were

presented in quiet. Hence, absolute FFT magnitudes were used to analyze the data. However, FFT peak magnitudes were measured relative to the noise floor in Chapters 8 & 9, when stimuli were presented in challenging listening conditions. For the remainder of this paper, the strength of envelope encoding (or FFR_{ENV}) will refer to the magnitude of FFT peak at 120 Hz while the strength of fine structure encoding (or FFR_{SPEC}) will refer to the FFT magnitude of the formant related harmonics. This dichotomy is based on findings from Aiken & Picton (2008) and Krishnan (2002) (see Chapter 2 for a detailed review). Additionally, narrow band spectrograms were used as a qualitative index of spectral content of the FFRs in the normal hearing and hearing impaired groups. Narrow-band spectrograms were obtained from FFR per subject per condition, and grand averaged for both groups.

3.6.3 Stimulus-Response Correlations

Differences in neural encoding between normal hearing and hearing impaired participants were also measured using a stimulus-response correlation analysis (Krishnan, Gandour, Smalt, & Bidelman, 2010), where the stimulus spectrum was compared with the FFR spectrum for each subject per condition. The stimulus-response spectral correlation technique ensured that FFR encoding of the complete harmonic structure of the entire stimulus is captured for analysis of group differences, yielding a correlation coefficient per subject per condition. The resulting correlation coefficient is expressed as a value between -1 and 1, where 1 represents a 100% stimulus-response correlation and -1 represents no correlation between stimulus and response. This analysis technique was used to estimate stimulus-response correlations for both envelope (F0) and TFS encoding

(F1 and F2-related harmonics). For envelope encoding, the original vowel stimulus was submitted to a Hilbert transform (rectification and low pass filtering) to extract the stimulus envelope. Stimulus-response correlations were performed on the extracted stimulus envelope and the FFR_{ENV} waveforms. For TFS encoding, FFR_{SPEC} waveforms were correlated with the stimulus waveform.

CHAPTER 4. EFFECT OF HEARING LOSS ON SUBCORTICAL REPRESENTATION OF ENVELOPE & TEMPORAL FINE STRUCTURE CUES IN STEADY-STATE SPEECH

4.1 Introduction

4.1.1 Motivation

Reduced speech perception (Dubno & Schaefer, 1992; Duquesnoy & Plomp, 1980; Nábělek et al., 1996; Nábělek, 1988; Nábělek et al., 1989; Summers & Leek, 1998) and degraded neural encoding (Miller et al., 1997; Woolf et al., 1981) consequent to SNHL has been well established. Recent research has focused more on the relative roles of envelope and temporal fine structure in the encoding of speech sounds and how it may explain the reduced speech perception abilities associated with sensorineural loss (Başkent, 2006; Henry & Heinz, 2012, 2013; Hopkins & Moore, 2011; Hopkins et al., 2008; Lorenzi et al., 2009; Lorenzi et al., 2006; Shamma & Lorenzi, 2013).

The basilar membrane can be viewed as a series of tonotopically organized overlapping band pass filters. Sharply tuned filters centered around high characteristic frequencies are located towards the cochlear base while broadly tuned low frequency filters with lower characteristic frequencies are located at apical locations of the cochlear partition. These cochlear filters are logarithmically spaced; however, harmonics in an incoming complex stimulus are linearly spaced. As a result, lower number harmonics are passed through separate auditory filters and are considered “resolved”. On the other hand,

multiple higher number harmonics are passed through high frequency auditory filters simultaneously, resulting in "unresolved" harmonics. Complex stimuli containing both low and high numbered harmonics arriving at the cochlea are decomposed by these "auditory filters" into envelope and temporal fine structure cues at the output of each filter (Moore, 2002). Envelope refers to "the slow variations in amplitude over time" whereas TFS refers to "rapid oscillations with rate close to the center frequency of the band" (Moore, 2008, p.399). Envelope and TFS outputs at each auditory filter are represented using a temporal coding scheme that hinges on variations in auditory nerve spike rates over time. Neural phase-locking encodes both envelope and TFS information up to 4-5 kHz in the auditory nerve (M. G. Heinz, Colburn, & Carney, 2001). For a complex tone, TFS information at the output of an auditory filter may be resolved (pure tone) or a complex waveform modulated at the F0 resulting from the interactions of the unresolved harmonics. Auditory nerve fibers phase-lock to the envelope of this modulated waveform as well as the underlying fine structure. Beyond 4-5 kHz, auditory nerve fibers mostly encode envelope cues represented by the modulation of unresolved harmonics, with a reduction in TFS encoding. The loss of TFS encoding with increasing frequency is attributed to the diminishing nature of neural phase locking at higher frequencies (Heinz et al., 2001; Henry & Heinz, 2013; Johnson, 1980; Joris & Yin, 1992). Studies using vocoded speech indicate that envelope cues presented alone provide adequate information about the speech signal in quiet (Shannon, Zeng, Kamath, Wygonski, & Ekelid, 1995) but the same does not hold true for challenging listening situations such as background noise, which require TFS cues (Qin & Oxenham, 2005).

Neurophysiologic studies in animals (M. Heinz, 2012; Henry & Heinz, 2012, 2013) and behavioral studies in humans (Baskent, 2006; Buss et al., 2004; Hopkins & Moore, 2011; Hopkins et al., 2008; Lorenzi et al., 2009, 2006; B. C. J. Moore, 2008; Shamma & Lorenzi, 2013; Swaminathan, 2010; Xu & Pfingst, 2008) have investigated the contributions of envelope and temporal fine structure cues to speech encoding and perception. The results of these studies, suggesting a differential effect of hearing loss on envelope and TFS encoding provides the primary impetus for the proposed experiment. Since both envelope and temporal fine structure information is preserved in the phase locked neural activity generating the FFR, it provides for an effective physiologic analytic window to examine the nature of neural encoding of both envelope and fine structure cues in NH individuals, and how this encoding is altered in individuals with SNHL. A more detailed account of the relative roles of envelope and TFS to both speech perception, and the neural encoding of complex sounds is developed in the following sections.

4.1.2 Psychophysical measures of temporal resolution in SNHL

Psychophysical studies examining the role of envelope cues through temporal resolution tasks such as gap detection paradigms or temporal modulation transfer functions suggest that envelope detection is equivalent or enhanced in HI as compared to NH listeners. This is illustrated by equivalent gap detection thresholds in both NH and HI listeners (Florentine & Buus, 1984), equivalent temporal modulation transfer functions (Bacon & Viemester, 1985) and better modulation detection in hearing impairment (Moore, 1996; Wojtczak, 1996). However, Fitzgibbons & Wightman (1982)

demonstrated poorer gap detection thresholds in hearing impairment as compared to NH at equal sensation levels.

Several studies (Tyler, Summerfield, Wood, & Fernandes, 1982.; Dreschler & Plomp, 1980) have demonstrated a strong correlation between measures of temporal resolution and speech recognition thresholds. Gap detection thresholds have found to be closely related to SRT in noise (Tyler et al., 1982) while SRTs in quiet is related to forward and backward masking effects (Dreschler & Plomp, 1980). Further, findings by Drullman, Festen & Plomp (1994) indicate that decreases in temporal resolution are accompanied by decreased consonant recognition. On the other hand, findings from Festen & Plomp (1983), Dubno & Dirks (1990) and Takahashi & Bacon (1992) have suggested no association between temporal resolution and speech recognition.

4.1.3 Behavioral measures of sensitivity to envelope & TFS in SNHL

Behavioral experiments (Füllgrabe, Meyer, & Lorenzi, 2003; Lorenzi et al., 2006) have demonstrated that envelope encoding is equivalent in NH and HI individuals. Lorenzi et al. (2006) studied differences in envelope and TFS processing between NH and HI (older and younger) subjects with moderate flat SNHL. Speech sounds were processed to extract speech containing envelope cues alone and TFS cues alone. Young and old HI subjects performed on par with NH subjects for unprocessed and envelope speech; however, significant deficits were observed in the TFS speech condition for the HI group. These findings suggest that TFS encoding is affected in hearing impairment even when age is controlled for, and plays a key role in speech perception. These findings are supported by Ardoint, Sheft, Fleuriot, Garnier & Lorenzi (2010) and Hopkins &

Moore (2007). Hopkins et al. (2008) compared TFS processing in NH and HI listeners by measuring speech reception thresholds to vocoded speech. TFS information was altered by changing the number of channels available. It was observed that HI subjects showed reduced benefit and ability to process TFS information as compared to NH listeners. Similar results were obtained by (Buss et al., 2004) who compared TFS processing ability (determined by detection of amplitude/frequency modulation) and speech recognition in NH and HI listeners. Results indicated that listeners with SNHL had poorer performance than NH listeners on the psychoacoustic task, suggesting that TFS encoding is affected in hearing impairment. It was also observed that performance on the psychoacoustic task was closely correlated with performance on the speech recognition task for the HI. Thus, the authors conclude that reduced TFS encoding has a strong influence on speech perception deficits in hearing impairment.

Summarily, psychophysical and behavioral experiments suggest that envelope encoding is enhanced in individuals with SNHL as compared to NH listeners; this enhancement may be a consequence of loudness recruitment. Envelope enhancement gives rise to a perceptual deficit in TFS encoding which results in poor speech perception abilities.

4.1.4 Neurophysiologic evidence of sensitivity to envelope & TFS in SNHL

The effects of sensorineural hearing impairment on envelope and TFS encoding at the single unit level appear to be stimulus dependent. For narrow band stimuli, TFS encoding appears to be largely unaffected, or only mildly affected by hearing loss. Harrison and Evans (1979) found no differences in phase-locking to pure tones (TFS)

presented in chinchillas with kanamycin induced OHC loss. Similar results were observed by Miller et al. (1997) in cats with NIHL, while phase locking to pure tones was only mildly affected in chinchillas with NIHL (Henry & Heinz, 2012). Contrary to these findings, Woolf et al. (1981) found a degradation in phase locking in response to low frequency pure tones at the level of the auditory nerve and cochlear nucleus in chinchillas with ototoxicity induced outer hair cell destruction.

Reduced TFS encoding consequent to degraded neural synchrony is more evident for broad-band stimuli in SNHL. In cats with NIHL, phase locking was observed to several frequency components and was not restricted to the fundamental/ formant regions alone. In general, phase locking in hearing impairment was described as "diffuse" and "broad-band" (Miller et al., 1997; Wong et al., 1998). However, conclusions from these studies only indicate degradations in TFS encoding abilities.

Kale and Heinz (2010) studied envelope and TFS encoding in chinchillas with NH and NIHL using single unit recordings from the auditory nerve in response to sinusoidally amplitude modulated (SAM) tones and single formant stimuli. Results indicated enhanced envelope encoding with no change in TFS encoding in the HI animals. Enhanced envelope was noted in the CF region corresponding to significant threshold shift (1-4 kHz); differences between NH and HI envelope encoding were reduced at CF regions where threshold shift was less. Further, the degree of envelope enhancement was greater for the more complex single formant stimulus than the SAM tones. Enhanced envelope encoding in hearing loss is attributed to auditory nerve response features such as high thresholds, steep rate level functions, low spontaneous rate (SR) and broadened tuning. Of these, only high thresholds and steep SR functions were the main factors in

enhancing envelope encoding. Fibers with low SR in NH animals did not show a corresponding enhancement nor did fibers with broadened tuning in the HI animals. This suggests that neither SR nor broadened tuning contribute significantly to envelope enhancement. Rate level functions may be described by C1 and C2 components. C1 components dominate the rate level function at low to moderate intensity levels while C2 components mediate rate level functions at higher intensities (80-90 dB SPL). The high level C2 component is resistant even in moderate to severe SNHL, while C1 responses are eliminated. Steep rate level functions reflective of C2 components in individuals with moderate to severe hearing loss may account for the enhanced envelope effects. Additionally, presence of only C2 responses is correlated with increased inner hair cell loss, while C1 responses were present in HI animals with relatively lesser inner hair cell involvement. Kale and Heinz (2010) infer that envelope enhancement is present to a lesser degree in mild-moderate hearing losses due to loudness recruitment while greater degree of enhancement may be seen in more severe losses due to the involvement of the C2 component.

Henry and Heinz (2012) extended this study to include stimuli presented in background noise. They found that while envelope encoding remains enhanced, significant deficits are observed in TFS encoding in the HI animals, stressing the importance of TFS cues in speech perception in adverse listening conditions. Henry and Heinz (2012) suggest that the decrease in neural phase locking for TFS cues in background noise is likely a function of wider than normal auditory filters. Additionally, findings from this experiment show a downward shift of CFs in chinchillas with NIHL,

such that high CF units that normally encode envelope information were observed to encode low frequency TFS information.

Moore (2003) provides an excellent summary of the physiological reasons that could contribute toward reduced TFS encoding in hearing loss. Possible physiological causes listed in this summary include reduced neural synchrony as demonstrated by the loss of synchrony capture in cats with NIHL (Miller et al., 1997), broader auditory filters, a loss of inhibition, shifts in frequency-place mapping and changes in relative phase responses on the basilar membrane.

4.1.5 Electrophysiological (FFR) evidence of sensitivity to envelope & TFS cues in SNHL at the subcortical level

Subcortical envelope and TFS encoding can be studied electrophysiologically using the FFR (Aiken & Picton, 2008; Krishnan, 2002; Anderson et al.,2013; Smalt et al., 2012). Several neurophysiologic studies have demonstrated that envelope information in complex sounds is encoded by interactions between higher unresolved harmonics at the level of the auditory nerve (Cariani & Delgutte, 1996; Meddis & O'Mard, 1997; Sayles & Winter, 2008). TFS cues are also encoded by neural phase-locking to unresolved harmonics provided the unresolved harmonics are within the limits of phase-locking harmonics (Cariani & Delgutte, 1996a, 1996b; Meddis & O'Mard, 1997; Young & Sachs, 1979). When frequencies of unresolved components exceed neural limits of phase-locking, auditory nerve fibers lock only to the envelope. Such encoding of envelope and TFS cues has also been documented at subcortical levels of neural encoding of complex stimuli. Specifically, it has been demonstrated that narrow-band noise centered at the F0

frequency in a complex tone containing unresolved harmonics does not affect the FFR component at F0 (Greenberg et al., 1987; Smalt et al., 2012). Results of these studies provide direct evidence that neural representation of F0, or envelope information, may be mediated by interaction of unresolved harmonics. Smalt et al., (2012) also demonstrated that the spectral FFR contains response peaks corresponding to frequencies of unresolved harmonics indicating that the FFR is capable to encoding temporal fine structure cues.

Plyler and Ananthanarayan (2001) examined the phase-locking ability of the human FFR to second formant transition in stop consonant stimuli in NH and HI listeners with mild to moderate SNHL. The basis for choosing formant transition as the stimulus feature of interest lay in previous perceptual data. Jacobson, Fant and Halle (1963) demonstrated that time varying features of speech play a major role in speech identification. Liberman, Delattre, Cooper, & Gerstman (1954) and Kewley-Port (1982) showed that NH listeners use the second formant transition to identify place of articulation for consonants. In contrast, HI listeners with mild to moderate SNHL were unable to utilize this information, causing reduced identification scores (Dorman, Marton, Hannley & Lindholm (1985). Plyler and Ananthanarayan (2001) chose a /ba-da-ga/ continuum with the second formant transition extending from 900 to 2300 Hz as the stimulus. In addition to the electrophysiological component, the study included a behavioral task involving stop consonant identification. Behavioral results indicated that overall, the performance of the HI group was significantly reduced as compared to the NH group across all stimulus levels. FFR data analysis revealed a shifting in the spectral peaks during formant transition for both NH and HI groups; however, the magnitude of frequency shift as measured by the FFR was always significantly greater in the NH than

in the HI group across all stimuli and intensity levels. These results were interpreted to suggest that the phase-locked activity in the HI individuals were not able to follow the frequency change presented in the formant transition. Further, the authors attributed such a persistent group difference at all presentation levels to degraded neural phase-locking. Findings from this study are also consistent with more recent perceptual and neurophysiologic studies that have demonstrated reduced TFS encoding in hearing loss. Further, correspondence between the behavioral and electrophysiological components of the experiment suggest that the FFR is capable of reflecting differences seen at the perceptual level in hearing impairment.

There is only one study (Anderson et al., 2013) that specifically addresses differences in subcortical envelope and TFS encoding of speech cues in hearing impairment. Based on perceptual and neurophysiologic evidence regarding envelope and TFS encoding, Anderson et al. (2013) predicted increased envelope encoding in HI participants. The stimulus used was a consonant-vowel /da/ presented in quiet, in noise, amplified (in quiet), amplified (in noise). The "amplified" conditions represented conditions where the stimulus was adjusted for audibility using an NAL algorithm, and were used only for the HI subjects. For the unamplified signal, results from the study indicated enhanced envelope encoding for the HI in noise but not in quiet; no group differences in TFS encoding were noted in quiet or noise. Envelope encoding was stronger in the HI group both in quiet and noise when the stimulus was adjusted for audibility, which was attributed to reduced inhibitory mechanisms in hearing impairment. Enhanced envelope encoding resulted in a relative deficit in TFS encoding. Findings for

enhanced envelope with hearing loss encoding are consistent with behavioral and animal studies; the lack of absolute TFS deficit in hearing impairment is not.

Results from these two studies suggest that the neural encoding of TFS is degraded in absolute terms (Plyler & Ananthanarayan (2001) and relative to envelope encoding (Anderson et al., 2013) in hearing impairment. However, effects of hearing impairment on envelope encoding were not examined by Plyler & Ananthanarayan (2001) (who focused on FFR encoding to formant transition, reflective of spectral FFR). Further, Anderson et al. (2013) showed no effect of hearing loss on TFS encoding, in contrast with data from Plyler & Ananthanarayan (2001), and inconsistent with the more extant perceptual and neurophysiologic literature.

4.2 Rationale

A general consensus emerges from across the studies reviewed above that representation of TFS is appreciably degraded with little or no change in the encoding of envelope cues in individuals with SNHL. Given that the phase-locked neural activity generating the FFR preserves both envelope and temporal fine structure information, it was reasoned that similar changes in the neural representation of envelope and TFS may be observed for the HI individuals presumably reflecting disruption in neural phase-locking in an ensemble of neurons, albeit from a measure reflecting neural activity at the level of the midbrain. The present experiment aims to characterize the nature of neural encoding of envelope and TFS cues in response to a steady state speech signal in NH and HI individuals using the FFR. Prior experiments (Plyler & Ananthanarayan, 2001; Anderson et al., 2013) have employed time-varying signals with conflicting results. In

order to examine effects of hearing impairment on a relatively simple, yet ecologically relevant stimulus, a steady state vowel was employed as the stimulus.

4.3 Methods

Please refer to Chapter 3 (General Methods) for general details of participant profiles, FFR recording protocols and data analysis techniques.

4.3.1 Participants

- Total number of participants: 44
- NH: 25 participants (male=8, female= 17); Age range: 21-55 years (*M*=27.72 years, *S.D.*=9.33 years
- HI: 19 participants (male=8, female= 17); Age range: 21-89 years (*M*=54.26 years, *S.D.*=19.40 years)

4.3.2 Stimulus

FFRs were recorded to a steady state, synthetically generated, English back vowel /u/ as in WHO'D (F0: 120 Hz, F1: 360 Hz, F2: 970 Hz, F3: 2667 Hz, F4: 3007 Hz). The FFR is recorded optimally for stimuli that have spectral content < 1500 Hz. The vowel /u/ was chosen as first two formants of the vowel occur at 360 Hz and 970 Hz, both less than 1500 Hz. Previous FFR experiments have demonstrated that the FFR can successfully encode F0 and F1-related harmonics in synthetic vowels such as /u/ (Krishnan, 2002).

4.4 Results

4.4.1 FFR waveforms in NH & HI

Grand averages of the FFR waveform representing stimulus envelope (FFR_{ENV}) and TFS (FFR_{SPEC}) for the NH and HI groups are shown in Figure 4.1. It can be clearly seen that slow, low frequency envelope related periodicity information is preserved in the FFR_{ENV} waveform whereas fast high frequency components are captured in the FFR_{SPEC} waveform for both groups. RMS amplitude in both the FFR_{ENV} and FFR_{SPEC} conditions appear considerably enhanced in the NH subjects as compared to HI subjects.

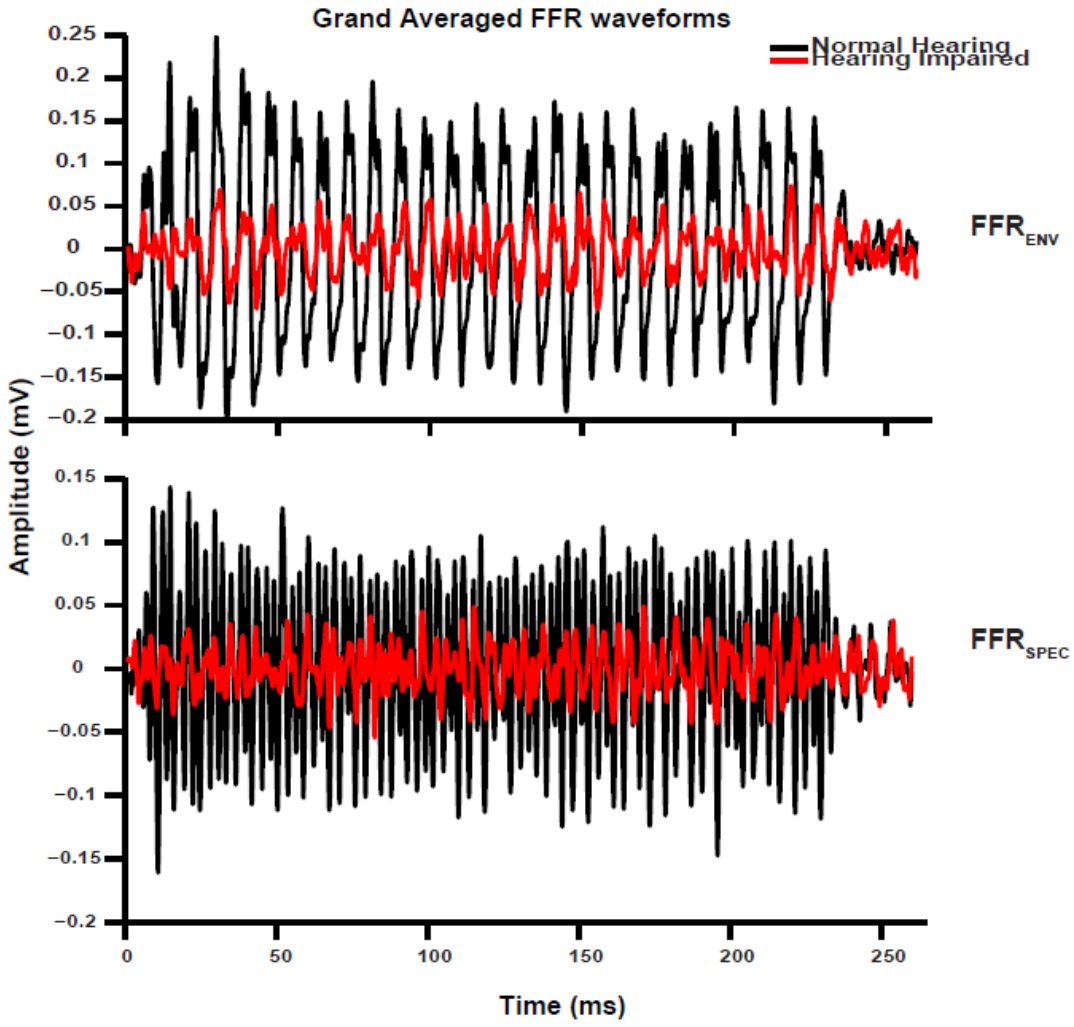

Figure 4.1: Grand averaged FFR waveforms in NH & HI. Grand averaged FFR waveforms are shown for envelope FFR (top) and spectral FFR (bottom). HI response (red) is superimposed on NH response (black).

4.4.2 Grand averaged autocorrelograms and spectrograms

Qualitative representations of the group differences in FFR_{ENV} and FFR_{SPEC} are provided in the grand averaged autocorrelograms and spectrograms derived for NH and HI (Figure 4.2). Stronger and clearer bands of phase locked activity are seen at the reciprocal of F0 in correlograms of the NH listeners than the HI listeners. While a band is seen at the F0 (120 Hz) in the grand averaged FFR_{ENV} spectrograms in both groups, the

NH group shows sharp activity at F0 whereas the band at 120 Hz appears weaker with a degree of spectral smearing in the HI group. Grand averaged spectrograms of the FFR_{SPEC} waveforms for the NH group shows a clear band at F1 (360 Hz); while a band is seen at 360 Hz in the HI as well, considerable spectral smearing marks the HI spectrogram.

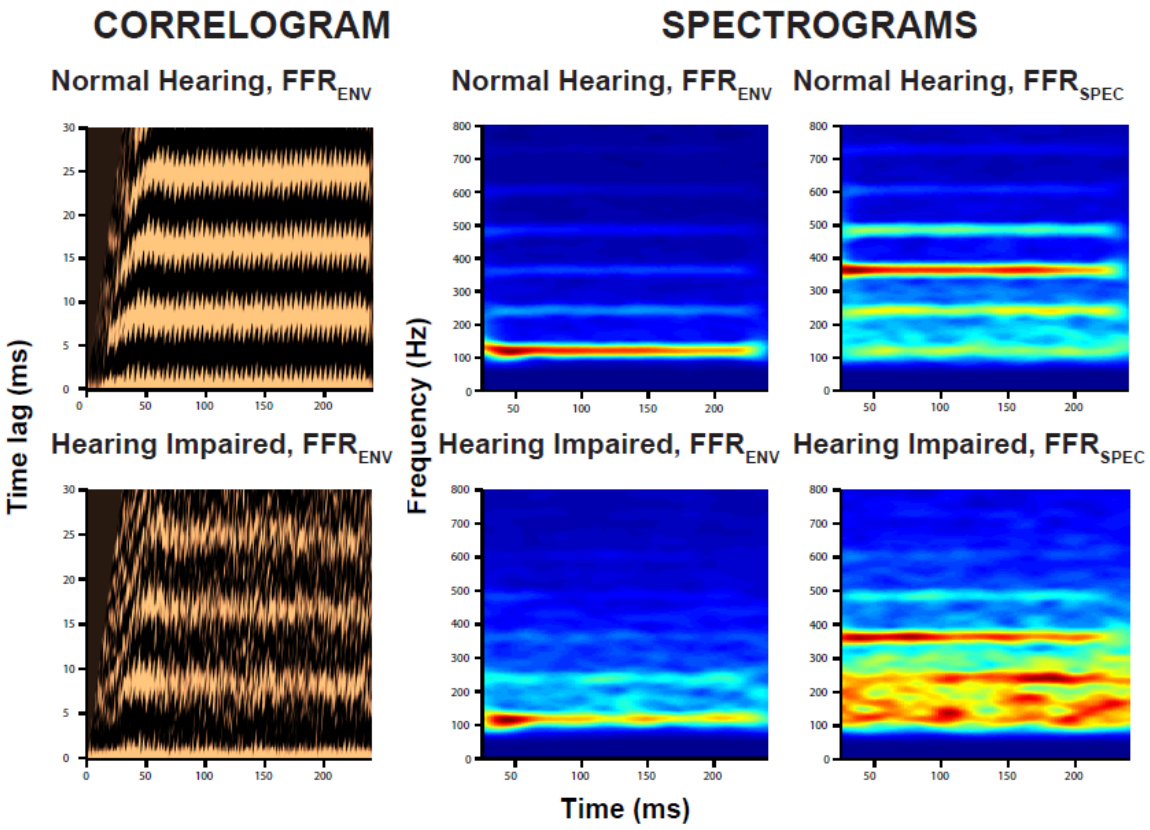

Figure 4.2.: Grand averaged autocorrelograms and spectrograms in NH & HI. Correlograms (left) & spectrograms (center & right) averaged across NH (top) and HI (bottom) subjects. Correlograms represent envelope FFR responses; spectrograms represent both envelope (center) and spectral (right) FFRs.

4.4.3 Temporal Analysis

Estimates of pitch strength or phase-locking to the F0 were obtained for both NH and HI participants by performing an autocorrelation analysis on the FFR_{ENV} waveforms.

A Kruskal-Wallis nonparametric ANOVA (used because rank observations failed homogeneity of variance) revealed a significant main effect of hearing loss on pitch strength [$\chi^2 = 20.1601$, DF=1, $P < 0.0001$]. Grand averaged autocorrelation functions for NH and HI are plotted in Figure 4.3.

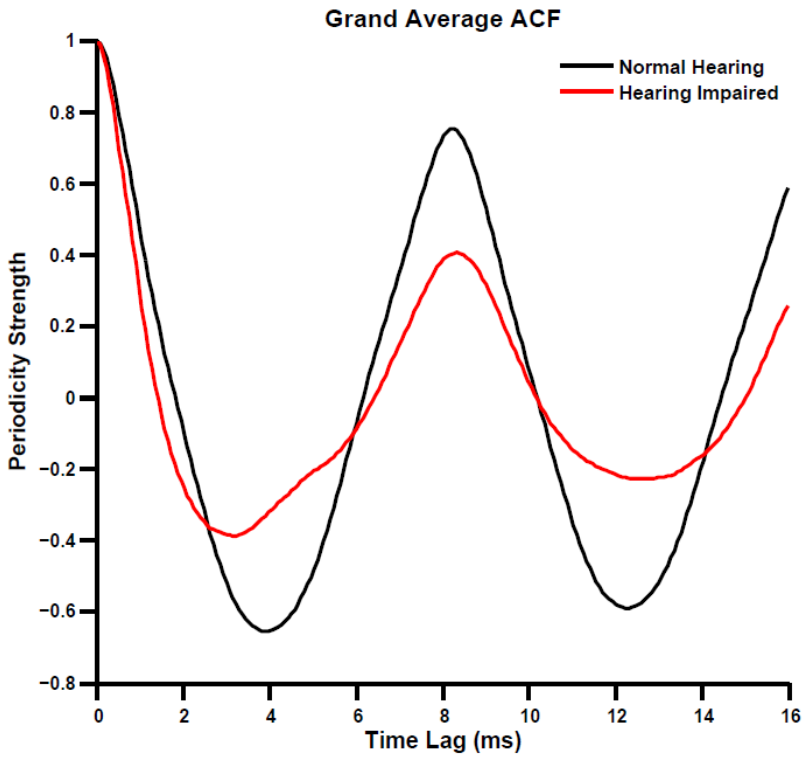

Figure 4.3.: Grand averaged auto-correlation functions (ACF) in NH (black) & HI (red).

4.4.4 Spectral representation

Grand averaged spectral data of FFR_{ENV} and FFR_{SPEC} are summarized in Figure 4.4. In the case of the FFR_{ENV}, a robust peak is seen at the fundamental frequency (120 Hz) in the NH group. While a peak at the F0 is preserved in the HI group, it is significantly reduced in amplitude as compared to the NH group. The group differences are preserved in the FFR_{SPEC} data. The NH group shows robust peaks corresponding to the stimulus harmonics (240 Hz, 360 Hz, 480 Hz, 840 Hz and 960 Hz); these peaks are

missing/extremely reduced in amplitude in the HI group. A dominance of harmonics close to F1 as well as relative reduction of non-formant related harmonics is seen in the FFR_{SPEC} data in the NH group ("formant capture and synchrony suppression"), but not in the HI subjects.

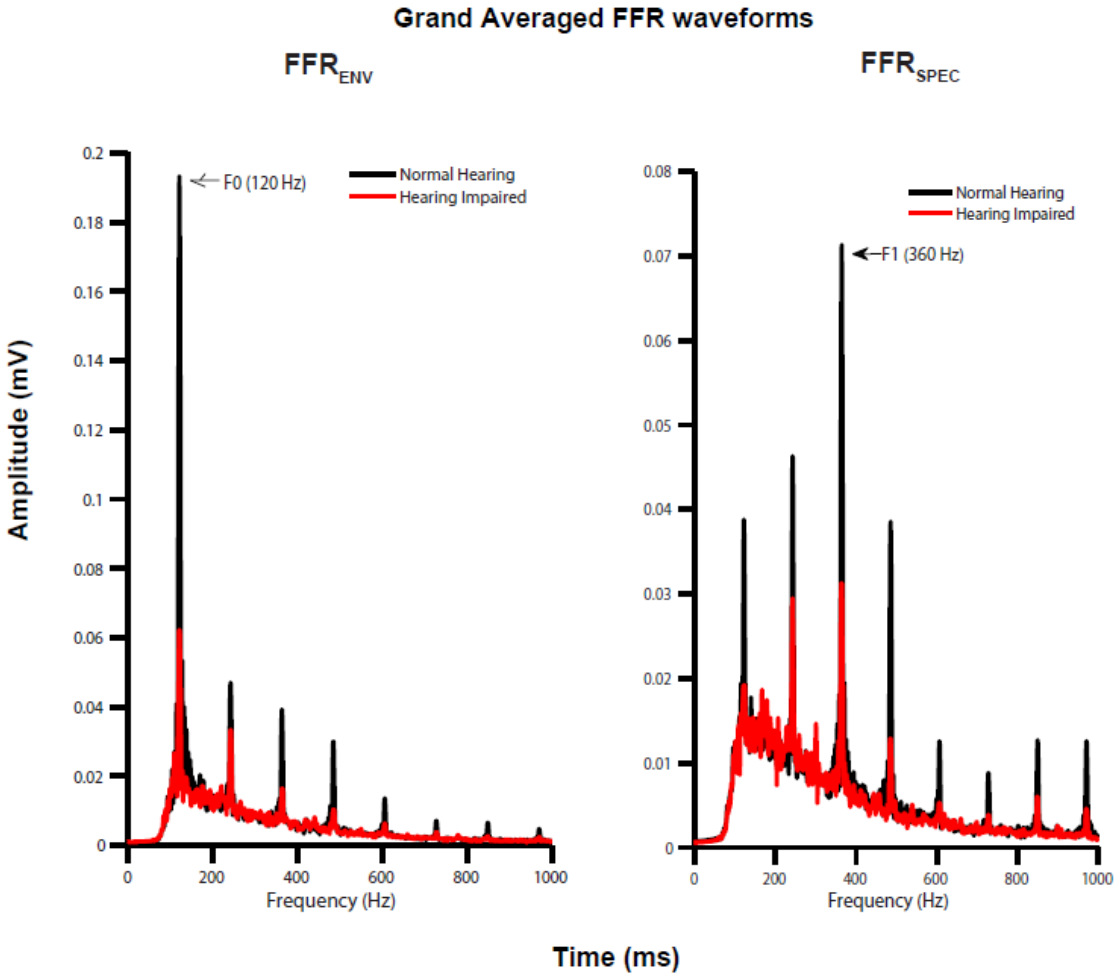

Figure 4.4.: Grand averaged FFTs in NH & HI. Grand averaged FFT data for FFR_{ENV} (left) and FFR_{SPEC} (right); HI FFT (red) superimposed on NH FFT (black).

4.4.5 FFT magnitudes at F0 & formant-related harmonics

The absolute magnitude of peak at the F0 (120 Hz) was measured in the FFT in the FFR_{ENV} condition to yield a measure of envelope encoding. FFT peak magnitudes at

harmonics 240, 360, 480, 840 and 960 Hz were averaged together to represent FFR-harmonic encoding. Differences in neural encoding of the stimulus in NH and HI subjects is evident at both F0 and response harmonics (Figure 4.5).

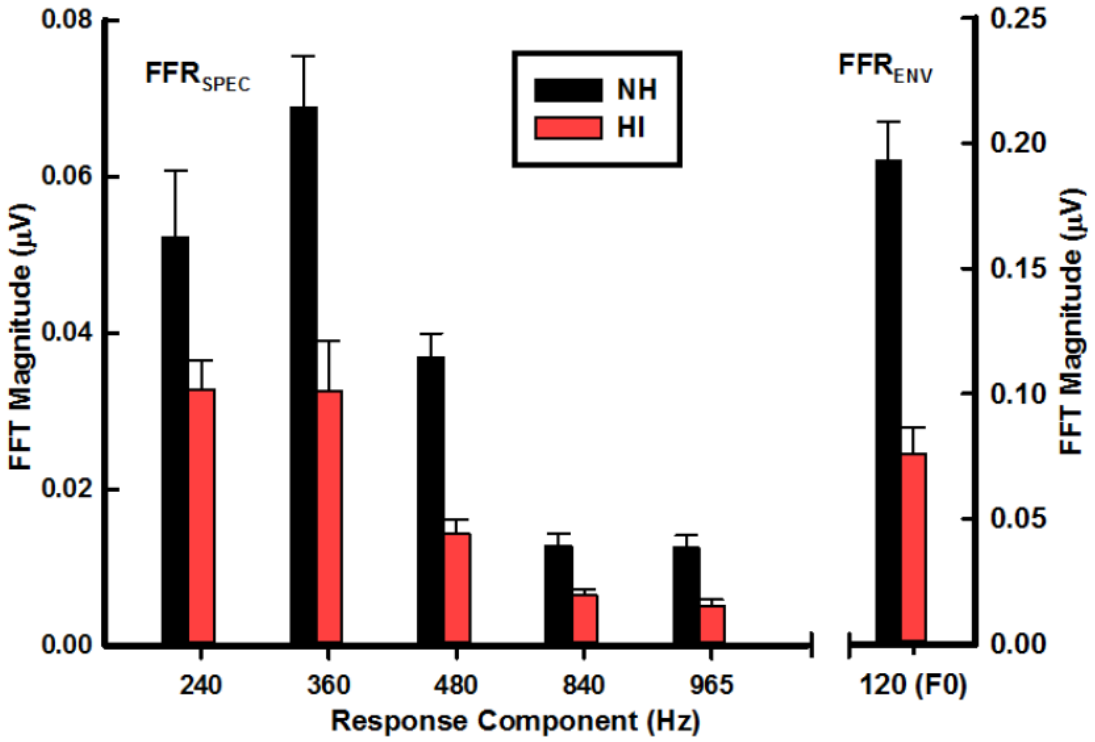

Figure 4.5: Mean FFT peak magnitudes in NH & HI. Mean FFT magnitude at the fundamental (FFR_{ENV}) (right) and formant-related harmonics (FFR_{SPEC}) (left) in FFRs obtained in response to the vowel /u/ in NH (black) and HI (red).

4.4.6 Statistical analyses at FFT peak magnitudes at F0 & formant-related harmonics

In order to satisfy the necessary model assumption of constant variance, a natural log transform was applied to the FFT response peak values at 120 Hz. The transformed response variables were used in the statistical analysis.

An analysis of covariance (ANCOVA) model was used to address the primary question: whether or not group differences are evident between NH and HI listeners with respect to spectral encoding of envelope (represented by F0-related peaks in the FFT). In many experiments studying differences between NH and HI participants, effects of hearing loss are often confounded by a co-varying factor: age. As hearing loss typically increases with advancing age, any differences between NH and HI participants must account for age. When studying hearing loss, age effects can be eliminated or reduced by the use of age-matched controls by inclusion of either younger HI subjects or older NH subjects, or by the use of statistical measures.

In the present experiment, most of the NH participants were younger (mean age: 27.72 years) and a majority of the HI participants were older (mean age: 54.26 years), leading to a moderate correlation between age and audiometric thresholds. To control for the observed age-audiogram correlation while examining effects of hearing loss, age was entered as a covariate in the ANCOVA model.

The ANCOVA model yielded a significant main effect for hearing loss ($F(1,39) = 4.51$, $P=0.0402$) and age ($F(1,39)= 0.12$, $P=0.73$). The interaction effect between age and hearing loss was also not significant ($F(1,39)=0.00$, $P=0.94$), indicating that the age effect, if any, is the same for both NH and hearing loss. The model was re-run after dropping the non-significant interaction term as a two way ANOVA model to yield a significant effect for hearing loss ($F(1,40)=24.86$, $P<0.0001$) such that F0 magnitude for NH ($M=0.1919652$, $S.D= 0.0758178$) was higher than the HI F0 magnitude ($M=0.0760947$, $S.D= 0.0450446$). The effect for age was not significant ($F(1,40)=0.14$,

P=0.71) in the reduced model either, indicating that age does not account for the observed group differences in F0 magnitude.

An ANCOVA model as used for the F0 data was applied to the averaged harmonic data. For the FFR harmonic data, none of the main effects (hearing loss: $F(1,39)= 0.86$, $P=0.36$; age: $F(1,39)=0.78$, $P=0.38$) or interaction effect between age and hearing loss ($F(1,39)=1.06$, $P=0.31$) were significant in the full model. The non-significant interaction term was dropped, and a reduced two way model rerun. There was a significant main effect of hearing group ($F(1,40)=17.41$, $P=0.0002$) and a non-significant age effect ($F(1,40)=0.12$, $P=0.72$).

In addition, FFT peak magnitudes at harmonics 240, 360 and 480 Hz were averaged together to represent F1 related FFR strength, while peak magnitudes at 840 and 970 Hz were averaged together to represent F2 related FFR encoding. Separate two independent sample t-tests yielded a significant effect of hearing loss for both F1-related ($t(42)=5.30$, $P<0.0001$) as well as F2-related FFR encoding ($t(42)=5.5$, $P<0.0001$)

Apart from grouping together the FFT peaks to obtain F1 related and F2 related harmonic values, separate two independent sample t-tests were used to determine group differences at each harmonic (i.e. at 120, 240, 360, 480, 840 and 960 Hz). Significant effects for hearing loss were observed at all response harmonics (120: $t(39.8)=6.32$, $p<0.0001$); 240: $t(32.2)=2.05$, $p=0.0487$); 360: $t(42)=3.88$, $p=0.0004$; 480: $t(37.5)= 6.48$,$p<0.0001$; 840: $t(35.5)=3.63$, $p= 0.0009$; 960: $t(34.9)=3.85$,$p=0.0005$), with better FFR harmonic representation in NH than HI.

4.4.7 Stimulus-response correlations

A Kruskal-Wallis nonparametric ANOVA (used because rank observations failed homogeneity of variance) revealed a significant main effect of hearing loss on stimulus-response correlations in the FFRENV condition [$\chi^2 = 21.4934$, DF=1, $P < 0.0001$]. The stimulus-response correlation was stronger for NH (M=0.57318, SD=0.016533) than HI participants (M=0.317889, SD=0.039874).

A one way ANOVA was used to analyze the stimulus-response correlations for the FFRspec condition. Similar to the FFR envelope, a significant effect of hearing loss was noted ($F(1,37)=15.19$, $P=0.0004$) with greater stimulus-response correlations for the NH (M=0.635295, SD=0.035772) as opposed to the HI FFRs (M=0.374847, SD=0.056067).

4.4.8 Variability within hearing impaired group

A cluster analysis was performed on the FFR data from 25 NH and 19 HI subjects to examine the distribution patterns of the two populations with respect to each other. By grouping together similar values of F0 and F1 neural encoding into two clusters, it was possible to identify the HI participants who performed as well as NH participants, thus isolating the high from the low performing HI subjects. Based on the cluster analysis, five of the nineteen HI participants were found to have neural envelope encoding values at par with the NH group. No clusters were formed on the basis of neural TFS encoding strength. Once these five subjects were identified, the HI group was divided into two subsets; subset 1 contained the five high performing subjects while subset two contained the remaining 12 low performing HI subjects. The cluster analysis was a more

exploratory statistical tool to study the patterns in the HI populations leading to the formulation of further specific questions involving these subgroups in the HI population were:

1. Is there a statistical difference between the strong performers and weak performers in the HI group?
2. How do these two subsets compare with the NH group?

To answer this question, a one way analysis of variance was conducted to examine statistical differences in FFR encoding (for F0 and F1) between the three groups: NH (n=25), high performing HI (n=5) and low performing HI (n=12). ANOVA yielded a significant main effect for hearing loss ($F(2,41)=45.42$, $P<0.0001$). Post hoc Bonferroni corrected multiple comparison testing of the means of all three groups indicated statistically significant differences between NH group and the low performing HI, as well as the high and low performing HI listeners (Figure 4.6 & 4.7). However, no differences were noted between the NH group and the high performing HI, consistent with results of the cluster analysis.

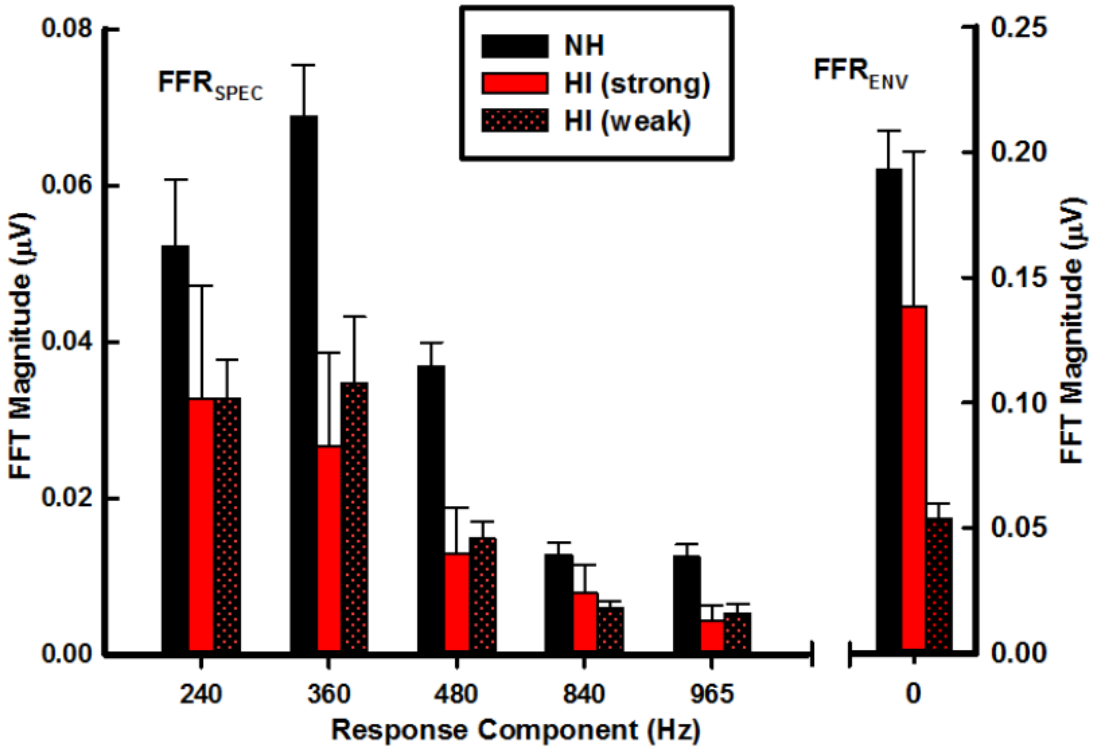

Figure 4.6: Mean FFT peak magnitudes in NH, strong HI & weak HI. Mean FFT magnitude at the fundamental (FFR_{ENV}) (right) and formant-related harmonics (FFR_{SPEC}) (left) in FFRs obtained in response to the vowel /u/ in NH (black), strong HI (red) and weak HI (dots).

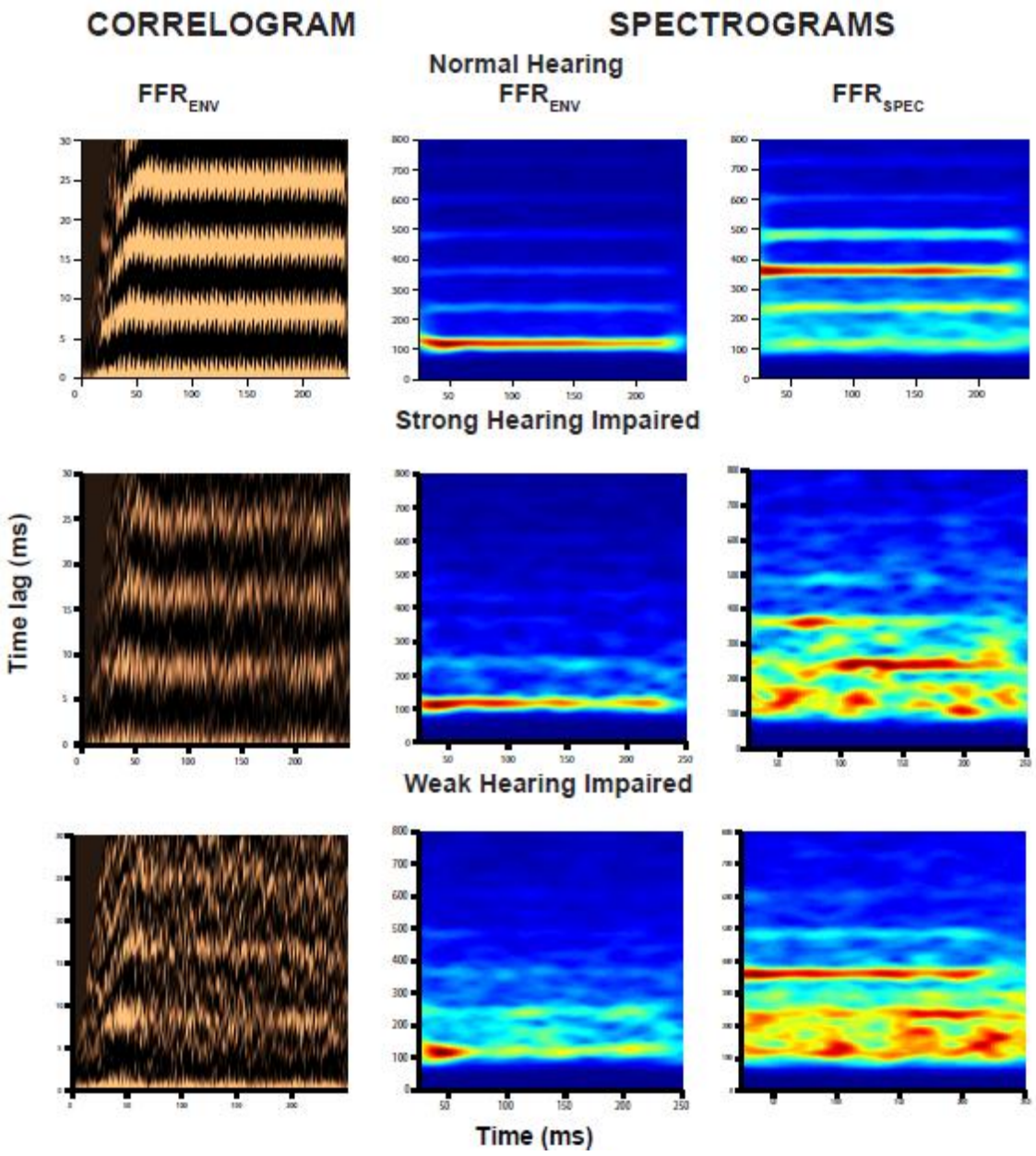

Figure 4.7: Grand averaged correlograms & spectrograms. Grand averaged correlograms (left) & spectrograms (center & right) averaged across NH (top) and HI (bottom) subjects. Correlograms represent FFR_{ENV} responses; spectrograms represent both FFR_{ENV} (center) and FFR_{SPEC} (right) FFRs.

4.4.9 Summary

Overall, the results from the current experiment can be summarized as follows:

- Neural encoding of envelope periodicity (FFR_{ENV}) as well as TFS (FFR_{SPEC}) was more robust with clear representation of formant related harmonics in NH compared to HI participants. Also, while the spectral profile for the NH subjects was characterized by enhanced spectral peaks for the formant related harmonics, the spectral profile for the HI subjects was flatter and did not show clear enhancement of spectral peaks corresponding to the formants. These results suggest that neural representation of both envelope and TFS is appreciably degraded in the HI subjects.
- There was no significant main effect of age for any of the spectral subcortical measurements of envelope and TFS encoding or any interaction between age and hearing loss, indicating that the observed group differences are a function of hearing loss and not aging effects.
- Neural encoding within the HI group showed a significant pattern of strong and weak performers. Interestingly, these differences in neural encoding were restricted to envelope cues. A detailed analysis on these strong and weak subsets is performed in Chapter 9.

4.5 Discussion

Neural encoding of envelope periodicity (FFR_{ENV}) as well as TFS (FFR_{SPEC}) was more robust with clear representation of formant related harmonics in NH compared to HI participants. Also, while the spectral profile for the NH subjects was characterized by enhanced spectral peaks for the formant related harmonics, the spectral profile for the HI subjects was flatter and did not show clear enhancement of spectral peaks corresponding

to the formants. These results suggest that neural representation of both envelope and TFS is appreciably degraded in the HI subjects.

4.5.1 Degradation of FFR TFS encoding is consistent with previous findings

The results for the observed group differences in temporal fine structure encoding are as expected, and consistent with findings from Plyler & Ananthanarayan (2001), who showed reduced formant transition encoding in the FFR in HI participants. Reduced TFS encoding in the FFR in quiet with hearing loss is also consistent with psychophysical studies (Hopkins & Moore, 2011; Lorenzi et al., 2006; Ardoint et al., 2010) as well as neurophysiologic experiments (Henry & Heinz, 2012). Reductions in TFS encoding have been attributed to decreased phase-locking (Miller et al., 1997; Woolf et al., 1981), changes in the relative phase of the response at different points along the basilar membrane (Ruggero, 1994; Carney, Heinz, Evilsizer, Gilkey & Colburn, 2002; Deng & Geisler, 1987; Loeb, White, Merzenich, 1983; Shamma & Klein, 2000), shifts in frequency-place mapping (Lieberman & Dodds 1984; Sellick, Patuzzi & Johnstone,. 1982) which could disrupt place dependent TFS encoding (Huss & Moore 2005; Moore 1982; Oxenham, Bernstein & Penagos, 2004), complex TFS with broader auditory filters (Moore 2008) and central changes such as a loss of inhibition (Moore, 2008).

4.5.2 Degradation of FFR envelope encoding is inconsistent with previous findings

The results showing degraded envelope representation are not consistent with previous behavioral and physiological findings. Specifically, most previous results show no change (Bacon & Viemester, 1985; (Lorenzi et al., 2006; B. C. J. Moore, 2008) or

even enhanced representation of envelope (B. Moore & Glasberg, 1988; Kale & Heinz, 2010).

Enhanced envelope detection in hearing loss has been attributed to the effects of loudness recruitment (B. Moore & Glasberg, 1988). However, at 80 dB SPL, envelope encoding mechanisms in the present study are likely already operating at sufficiently high levels where recruitment effects, if any, should be manifested. According to Kale and Heinz (2010), envelope enhancement may be determined by examining rate level functions, which are described by two components: C1 and C2. The C1 component dominates the rate level function at low to moderate intensity levels while C2 component mediates rate level functions at higher intensities (80-90 dB SPL). The high level C2 component is resistant even in moderate to severe SNHL, while C1 responses are eliminated. Steep rate level functions reflective of C2 components in individuals with moderate to severe hearing loss may account for the enhanced envelope effects. Additionally, presence of only C2 responses is correlated with increased inner hair cell loss, while C1 responses were present in HI animals with relatively lesser inner hair cell involvement. Kale & Heinz (2010) infer that envelope enhancement is present to a lesser degree in mild-moderate hearing losses due to loudness recruitment while greater degree of enhancement may be seen in more severe losses due to the involvement of the C2 component. Hence, listeners with mild to moderate hearing loss (less loss of non-linearity) may not demonstrate as great of an enhanced envelope encoding as those with severe to profound losses (greater loss of non-linearity). It is possible to extend this line of reasoning to data from the present study as all participants had mild to moderate SNHL, which would predict a comparatively lesser degree of envelope enhancement. However,

it does not explain why the mild enhancement noted in animals with mild-moderate hearing loss as compared to NH subjects by Kale & Heinz (2010) is not seen in the present study. Also, the FFR represents ensemble neural activity and therefore represents the summed neural activity of population of neurons with different thresholds and rate level functions which could obscure the enhancement observed for selective single units with steep rate level functions and higher thresholds. Alternatively, it is possible that the reduced envelope encoding in the HI FFR data in the current experiment is more reflective of a local (that is, in the population of neural elements generating the FFR in the rostral brainstem) general disruption in the temporal pattern of neural activity consequent to a peripheral hearing loss that has adverse effects on neural timing (and therefore synchronization of neural activity) that is cumulative along the auditory neuraxis. The relatively greater deterioration of TFS encoding compared to the envelope encoding observed here supports this view. Specifically, timing disruption via temporal jitters may have more pronounced effects on faster changes (TFS) than slower changes (envelope).

Reduced envelope encoding in HI listeners obtained in this study is not consistent with HI FFR data from Anderson et al. (2013). Anderson et al. (2013) found no differences in envelope encoding in NH and HI in quiet for the unamplified condition, the stimulus condition most comparable to that used in the current experiment. Further, Anderson et al. (2013) reason that enhanced FFR envelope encoding noted in the quiet (adjusted audibility) conditions in the HI group may be attributed to an imbalance between inhibitory and excitatory mechanisms. Reduced inhibitory and enhanced excitatory mechanisms subsequent to hearing loss have been documented in animal

studies (Vale & Sanes, 2002; Willott, 1981). Anderson et al. (2013) also discuss the possibility that wider auditory filter bandwidths in hearing impairment may allow a greater amount of energy through, which in turn may be represented as enhanced envelope measures. However, this argument is contradictory to the notion that increased auditory filter bandwidths in hearing impairment lead to a distorted representation of the input signal.

4.5.3 Factors causing degraded phase-locking

The FFR reflects phase-locking ability from a population of neural elements in the auditory brainstem. Therefore, a reduction in FFR strength for envelope and TFS cues with hearing impairment indicates a reduction in the ability of brainstem neurons to fire at intervals corresponding to the pitch of the incoming signal (Miller et al., 1997; Woolf et al., 1981).

Factors that could play a role are in the degradation of neural representation of envelope and TFS include audibility, disrupted neural phase-locking consequent to hearing loss; disruption in neural timing; reduced frequency selectivity that may disrupt phase-locking

In the following sub-sections, each of these potential reasons are addressed in the context of the results from the current experiment, with supporting findings from behavioral, modeling and single unit experiments.

4.5.3.1 Role of audibility

It is possible that the observed group differences for envelope and temporal fine structure encoding are due to a lack of audibility for the HI participants. As FFRs were measured at a fixed sound pressure level in both NH and HI subjects, audibility effects cannot be ruled out. The contribution of audibility to envelope and temporal fine structure is addressed in Chapter 5. Based on findings from other subcortical studies of hearing impairment, it is possible that there are differential effects of amplification on envelope and TFS encoding. Plyler & Ananthanarayan (2001) included multiple presentation levels in their study, and found no statistically significant improvement in neural encoding of TFS as a function of intensity. Anderson et al. (2013) included an "amplified" condition, which adjusted the stimulus for audibility for the HI group; there were no differences between the results for the quiet condition and the amplified condition for TFS, but an enhancement in envelope encoding was noted. Neural phase-locking at the single unit level in HI cats did not improve as a function of stimulus sound pressure level (Woolf et al., 1981).

Behavioral experiments examining temporal resolution in NH and HI listeners have yielded mixed results. Gap detection and temporal modulation transfer function studies have demonstrated similar performance by both NH and HI individuals when audibility was restored by testing at equal SLs (Bacon & Viemester, 1985; Florentine & Buus, 1984) as have speech recognition studies (Dubno & Dirks, 1984). On the other hand, studies by Fitzgibbons & Wightman (1992) and Moore & Glasberg (1987) have shown that differences between NH and HI listeners continue to persist even when audibility is adjusted for. Both neurophysiologic (Henry, Kale, Scheidt, & Heinz, 2011;

Wong et al., 1998; Woolf et al., 1981) and electrophysiological (Plyler and Ananthanarayan, 2001; Anderson et al., 2013) experiments examining frequency resolution (i.e. representation of fundamental frequency and harmonics) have repeatedly established that audibility does not entirely account for group differences between NH and HI listeners.

Based on results from these previous studies, it is likely that audibility is not the only factor causing the observed group differences, at least for TFS encoding. However, comparisons at equal sensation levels are needed before the role of audibility can be ruled out.

4.5.3.2 Disrupted phase-locking precision

It is well established in the literature that synchronous firing of neural elements is required for a robust and accurate encoding of the incoming signal. Pitch encoding up to 5 kHz is regulated primarily by temporal mechanisms. While the temporal theory is unable to account for high frequency encoding due to a reduction of neural phase locking with increasing frequency, temporal mechanisms likely play a key role in encoding low frequency stimuli as used in the present study. Wakefield & Nelson (1985) incorporated phase locking as a part of the Goldstein & Srulovicz (1977) auditory model, and predicted poorer FDLs in HI individuals when the effect of hearing loss was modeled as reduced neural phase-locking. Computational models thus implicate a disruption in neural synchrony in HI pitch perception. A disruption in neural phase locking precision may contribute towards reduced FFR encoding seen in HI subjects.

Disrupted neural phase-locking in hearing impairment has also been shown in single unit data from Miller et al. (1997) and Woolf et al. (1981). Woolf et al., (1981) found significant reductions in neural phase locking to pure tones at the level of the auditory nerve and cochlear nucleus in chinchillas with NH and ototoxicity induced outer hair cell destruction. Further, the differences in neural phase locking persisted at higher sensation levels where audibility was eliminated as a contributing factor. Findings from this study indicated that neural synchrony was disrupted in a frequency dependent pattern consistent with audiometric thresholds.

In the present experiment, the strong formant-related harmonic encoding, or "synchrony capture" observed in NH FFRs (Krishnan, 2002) was present in NH participants but reduced/missing in the HI FFR. Reduced or absent phase locking to formant related harmonics in hearing impairment at the brainstem level has its origins at the level of the auditory nerve. The phenomenon of synchrony capture was first described by Miller et al. (1997), where single unit data in response to a vowel sound was compared between NH and HI cats at three presentation levels. Level dependent changes in phase-locking to formant frequencies were observed. Apart from the formant frequency, phase-locking was noted at multiple frequencies close to the formant frequency at the lowest presentation level. With increasing level, phase-locking to the formant improved (as predicted); in addition, "synchrony capture" was noted, i.e. response components surrounding the formant frequency diminished and disappeared. However, the cats with NIHL had significantly reduced/absent synchrony capture. The phenomenon of synchrony capture has also been documented in the FFR to steady state vowels including /u/ in NH listeners (Krishnan 2002). Consistent with FFR findings (Krishnan, 2002), an

increase in neural encoding of formant related harmonics was noted in the NH subjects; also consistent with single unit data (Miller et al., 1997), synchrony capture was missing/reduced in the HI FFRs. Loss of synchrony capture in HI participants provides evidence supporting reduced precision in subcortical neural phase locking in hearing impairment.

Tonotopic remapping may occur in high frequency hearing loss, in both the IC and the auditory cortex, causing a shift in neurons with high CFs (>20 kHz) towards middle frequencies (10-15 kHz), which shift to even lower frequencies when hearing loss extends towards the middle frequencies. When neurons on adjacent healthy portions of the basilar membrane start "covering for" neurons in damaged regions, normal neural encoding is disrupted due to excess neuronal excitation for certain stimuli. This downward shift of high frequency CFs and an associated decrement in neural phase locking has been demonstrated by Henry & Heniz (2012) in chinchillas. Per Willott (1981) inhibitory mechanisms in the mouse IC are sensitive to high frequencies; hence high frequency hearing loss reduces activation of these inhibitory mechanisms. The balance between excitatory and inhibitory mechanisms required for modulating neural responses during encoding of broadband stimuli is disrupted in the case of high frequency hearing loss in mice, where neural responses become larger than normal due to a bias towards excitatory mechanisms and a lack of inhibition. Neural representations of pitch may be distorted as a result of these plasticity effects.

4.5.3.3 Reduced phase-locking due to reduced frequency selectivity

Reduced FFR encoding to the frequency components of the speech signal in HI subjects in the present study may be attributable in some part to degraded phase locking consequent to reduced frequency selectivity in hearing loss. Reduced frequency selectivity is one of the typical consequences of SNHL, occurring due to wider auditory filter bandwidths. Broadly resolved frequency components may cause diffuse patterns of phase locking to a wide frequency range, as opposed to "tight" phase-locking confined to a narrow band of frequencies in NH subjects.

Leek and Summers (1996) investigated the effects of decreased frequency selectivity in vowel perception in noise in NH and HI listeners. Spectral contrast, or the difference between peaks and valleys of formant frequencies and auditory filter bandwidths were measured in both groups. Results indicated that greater spectral contrasts are required by the HI subjects who have reduced frequency selectivity as indexed by wider auditory filters at 2 kHz.

The fundamental frequency in the stimulus used in this experiment was located at 120 Hz while the first formant was located at 360 Hz. A majority of the HI subjects had good or relatively good low frequency hearing. The average audiometric threshold at 250 Hz and 500 Hz was and respectively. FFR encoding to low frequency cues was reduced even with audiometric thresholds that classify within the normal or near-normal category. This finding suggests that reductions in frequency selectivity alone cannot account for the effects of hearing loss seen in the data from the present study, and that alternate explanations must be explored.

That impaired frequency selectivity is not always predictive of degraded pitch perception in SNHL has been demonstrated in several psychophysical (Simon & Yund (1993); Tyler et al., 1983; Moore & Peters, 1992) and speech perception experiments (Lorenzi et al., 2009). Simon & Yund (1993) observed differences in FDL measures in ears with the same pure tone threshold, and similar FDLs in ears with different pure tone thresholds; as these measurement comparisons were made *between* ears of subjects with bilateral hearing impairment, the effects of between subject variability were eliminated. FDLs and psychophysical tuning curves indexing frequency selectivity were poorly correlated in individuals with hearing impairment (Tyler et al., 1983) as were FDLs and auditory filter bandwidths obtained using notched noise method (Moore & Peters, 1992; Glasberg & Moore, 1990).

Speech perception results from Lorenzi et al. (2009) have shown that TFS encoding to nonsense syllables is significantly affected in HI individuals who have normal or near normal audiometric thresholds at frequencies below 1.5 kHz. In addition, the stimuli used by Lorenzi were low pass filtered, thus eliminating any components greater than 1.5 kHz. TFS deficits in HI listeners despite the hearing loss configuration and stimulus design lend further support to mechanisms other than reduced frequency selectivity.

These results are further supported by Horwitz, Dubno, & Ahlstrom (2002), who demonstrated a reduced ability to process low pass filtered speech in those with high frequency hearing loss. Similar findings were seen in the study by Smoski & Trahiotis (1986), where high frequency hearing impairment resulted in a reduced ability to detect inter aural time differences in low frequency tones. While there have been other studies

(Ching et al., 1998; Hogan & Turner, 1998) that show reduced TFS processing with high frequency loss, these are usually restricted to subjects with hearing loss greater than 60 dB. However, Hopkins et al. (2008) found that several subjects with hearing loss less than 60 dB who were unable to process high frequency components of speech; thus reduced ability to process TFS information may be associated with high frequency hearing loss, even in mild to moderate hearing impairment. Hopkins and Moore (2010) specifically investigated the effect of frequency selectivity on TFS processing ability in HI subjects by correlating ERBs with TFS encoding of complex tones while controlling for audiometric thresholds. The authors found no significant correlations between TFS encoding and ERBs for any center frequency, thus indicating that TFS encoding is not affected by frequency selectivity. Further strengthening this argument, Hopkins and Moore (2010) found that TFS encoding was affected even for subjects with normal low frequency hearing normal ERB values at low center frequencies but impaired high frequency hearing. Kale and Heinz (2010) also found similar results in single unit data, where envelope and TFS encoding in chinchillas with NIHL was unrelated to their frequency selectivity. Hence, reduced frequency selectivity in HI subjects cannot wholly account for reduced TFS encoding. While reduced frequency selectivity cannot be completely ruled out, alternate mechanisms (impaired temporal processing, reduced number of auditory nerve fibers) may also contribute towards reduced TFS encoding.

4.5.3.4 Role of unresolved harmonics and high frequency hearing loss

Several studies have demonstrated that envelope information in complex sounds is encoded by interactions between higher unresolved harmonics (Cariani and Delgutte, 1996a, 1996b; Meddis & O'Mard, 1997; Sayles and Winter, 2008).

Broader cochlear filters in hearing loss reduce frequency resolution (Glasberg & Moore, 1986; Moore, 1998); the loss of frequency resolution can cause deficits in TFS cues available and render the HI listener dependent on envelope cues arising as a result of modulation of unresolved harmonics (Moore & Carlyon, 2005; Moore & Moore, 2003). F0 discrimination in hearing impairment may be influenced to a great extent by the contribution of high frequency regions from 1200-2400 Hz (Arehart, 1994; Moore & Glasberg, 1990). HI subjects were shown to have better F0 discrimination for harmonic complexes containing mid-high frequency components greater than 1600 Hz as opposed to complexes containing lower frequency harmonics (Arehart, 1994). Moore & Glasberg (1990) found improved F0 discrimination for F0=200 Hz in HI subjects for harmonic complexes with components 6-12 as opposed to 1-12. On the other hand, harmonic components 3-5 play a major role in determining pitch for NH listeners (Plomp, 1967; Ritsma, 1967). Hence it is possible that NH and HI listeners make use of different frequency regions in pitch discrimination tasks. In a F0 discrimination task conducted by Summers & Leek (1998), correlation analyses of F0DL with different audiometric thresholds indicated the best correlation with threshold at 2 kHz in the HI listeners. All HI subjects in the study had near NH below 1000 Hz and moderate hearing loss above 1000 Hz. Based on this result, the authors reason that high frequency regions act as important contributors toward F0 discrimination in HI listeners, as opposed to low

frequency regions in NH listeners. The stimuli used by Summers & Leek (1998) for F0 discrimination were similar to those used in the present study: steady state synthetic vowels with an F0 at 120 Hz. Based on findings from Summers & Leek (1998), it is possible that poorer audiometric thresholds at higher frequencies contribute towards the reduced envelope encoding observed in HI subjects. Average pure tone thresholds at low frequencies were better than at high frequencies for the HI group. Hence, degraded FFR encoding to low frequency components in hearing impairment even when low frequency thresholds are normal or near normal may be due to remote effects from impaired high frequency regions, which have been implicated in poorer F0 discrimination seen in hearing impairment.

4.5.3.5 Effects of aging and hearing impairment on neural speech encoding

One of the confounding factors in the current experiment involves the relationship between age and audiometric thresholds for NH and HI subjects. The average age of the NH subjects was 27.72 and 54.26 years for the HI group. The average pure tone averages (.5,1,2 kHz and 2,3,4 kHz) were 9.1 and 7.9 dB HL for the NH group and 32.89 and 40.08 dB HL for the HI group. An analysis of covariance model, where age was entered as a covariate, was used to circumvent the age-audiogram confound. The effects of age were found to be not significant in the current study, eliminating the contribution of age towards the differences seen between the NH and HI populations.

The lack of age effects in the current experiment is consistent with findings from (Clinard, Tremblay, & Krishnan, 2010). Clinard et al. (2010) inferred that age related

effects are not seen in the FFR for low frequencies. As both the F0 (120 Hz) and F1 (360 Hz) in the stimulus in the current experiment were below 500 Hz, it is reasonable to assume that the observed differences between NH and HI participants are not influenced by the differences in their ages.

Additionally, an overall trend observed in findings from various perceptual studies is that age effects in speech perception are not usually present in quiet environments with adequate audibility, or for simple auditory tasks, but become evident in challenging listening conditions such as reverberation and background noise. Gordon-Salant (2005) and Pichora-Fuller & Singh (2006) provide excellent reviews of various investigations that address age related changes in auditory tasks. As the stimuli in the current experiment were presented in quiet, it is unlikely that age effects are influencing the results.

4.5.3.6 Combined effects contribute to decreased phase-locking in HI

Decreased audibility as indexed by poorer audiometric thresholds and poor frequency selectivity are hallmarks of SNHL. However, deficits in neural encoding of speech in HI individuals persist even when audibility is restored. Neural phase locking is degraded in response to stimulus frequencies much removed from the region of reduced frequency selectivity on the cochlea. Hence, a loss of audibility or poor frequency selectivity do not entirely account for differences observed in speech perception abilities between NH and HI listeners. Decreased neural phase-locking precision or a in conjunction with abnormal basilar membrane phase responses and reduced number of

auditory nerve fibers may also contribute towards the challenges in speech encoding observed in hearing impairment. Overall it is clear that the effect of hearing loss on subcortical speech encoding cannot be attributed to one single underlying cause; rather, it is likely the result of a combination of the different factors discussed above.

4.6 Conclusions

Overall, the findings from the present experiment may be summarized as follows:

- Neural phase locking of fundamental as well as formant related harmonics is reduced in HI subjects as compared to NH subjects, when stimuli are presented at a single intensity level.
- The effect of hearing loss is not confounded by age differences between NH and HI subjects, when the stimulus is presented in quiet.
- Differential FFR strength for envelope and TFS encoding were not observed in this experiment, contrary to recent FFR findings (Anderson et al., 2013) and numerous psychophysical experiments.
- Reduced phase locking in hearing impairment is likely due to a complex interplay between various factors such as reduced audibility, poor frequency selectivity and impaired temporal synchrony.
- Further investigation at multiple presentation levels and signal to noise ratios is required to gain a better understanding of level dependent changes in envelope and TFS encoding in hearing impairment, addressed in Chapter 5.

CHAPTER 5. ROLE OF AUDIBILITY IN SUBCORTICAL NEURAL ENCODING OF ENVELOPE & TFS CUES

5.1 Introduction

5.1.1 Motivation

According to Plomp & Duquesnoy (1982), hearing impairment is determined by two major factors, which they referred to as the "attenuation factor" and the "distortion" factor. Attenuation refers to the reduction in audibility of the target and competing signals. Distortion consists of the remaining speech deficit after audibility is restored (Plomp & Duquesnoy, 1982; Leek & Mollis, 2009). Speech perception deficits in listeners with SNHL are not entirely attributable to a lack of audibility. However, comparisons between NH and HI subjects are often confounded by differences in audiometric threshold and stimulus presentation levels (Dubno & Schaefer, 1991). When stimuli are presented at equal SPLs to NH and HI groups, the HI participants hear the stimulus at a much lower sensation level (SL). Lower SLs render the stimulus much softer to the HI listeners, bringing up the much debated and investigated issue of audibility. In other words, will the performance of the HI individuals be on par with the NH individuals if the stimulus was adjusted for audibility?

Equal audibility can be achieved by various techniques such as additive masking noise (Dubno & Schaefer, 1992; Florentine, Fastl, & Buus,1988; Florentine, Reed, Rabinowitz, Braida; Durlach, & Buus, 1993) or multiband amplitude expansion

(Villchur 1973, 1974; Moore & Glasberg, 1993), both of which simulate effects of hearing loss in NH listeners. The additive masking noise technique recreates features of SNHL, including but not restricted to increased thresholds, in NH listeners and allows for comparisons between NH and HI subjects at equal SLs and equal SPLs. The multiband amplitude expansion approach involves attenuating the input signal to replicate the effects of SNHL (Desloge, Reed, Braida, Perez, & Delhorne, 2011).

Level dependent changes in speech sound encoding in NH and HI listeners are also investigated by presenting stimuli at a wide range of intensities. As HI subjects may experience loudness recruitment, it is not always be feasible to use high intensity stimuli for this group. Further, frequency resolution decreases as a function of stimulus presentation level in both the healthy and impaired auditory systems, owing to wider auditory filters at higher intensities (Edwards, 2004). Hence, there is an added unfavorable effect of level dependent auditory filter bandwidth broadening when stimuli are presented at high intensity levels in HI listeners in an attempt to make the stimulus audible (Edwards, 2004).

In order to tease apart the effects of reduced audibility and "distortion effects" in hearing impairment, it is essential that comparisons between NH and HI subjects be carried out at equal audibility. While several behavioral (Bacon et al., 1998; Buus & Florentine, 1985; Ching et al., 1998; Dubno & Schaefer, 1992; Duquesnoy & Plomp, 1983; Fitzgibbons & Gordon-Salant, 1987; Fitzgibbons & Wightman, 1982; Gagné, 1988; B. Moore & Glasberg, 1988; Peters, Moore, & Glasberg, 1995; Plomp, 1964; Plomp, 1964; Summers & Leek, 1994, Tyler et al., 1982) and neurophysiologic (Heinz & Young, 2004; Henry et al., 2011; Wong, Miller, & Calhoun, 1998) studies address the

confounding effects of audibility in experiments investigating effects of hearing loss on speech encoding and perception, there is a dearth of experiments that systematically investigate level dependent changes in neural representations of speech in the human HI system. The current experiment investigates the effect of hearing loss on neural encoding of envelope and TFS information as a function of stimulus presentation level, facilitating comparisons at equal SPLs and equal SLs. The following section lays the foundation for the current experiment, by describing results from behavioral studies and animal models with regard to the audibility confound and existing evidence of level dependent changes in neural representation of speech sounds as reflected by the FFR.

5.1.2 Psychophysical studies examining the role of audibility in envelope & TFS cue perception in SNHL

Psychophysical studies have addressed the issue of audibility in hearing impairment yielding mixed results.

Bacon & Viemester (1985) found that unaided temporal modulation transfer functions (TMTF) obtained in HI listeners were reduced in sensitivity to modulation with a steeper slope at high modulation frequencies. When high frequency hearing loss was simulated in NH subjects using adding high pass masking noise and low pass filtering the signal, TMTFs were similar to the unaided HI TMTF. Further, TMTFs in HI individuals were similar to NH TMTFs when presented at the same SL (Bacon & Gleitmann, 1992; Moore, Peters, & Glasberg, 1992). Results from Strickland and Viemester (1997) support the relationship between increased audibility and better temporal resolution in HI listeners. Florentine and Buus (1984) reported similar gap detection thresholds in NH and

HI listeners when stimuli were presented at equal SLs. B. Moore and Glasberg (1988) measured gap detection thresholds for broadband noise and sinusoidal markers in seven subjects with unilateral SNHL. Comparisons between normal and impaired ears were made within each subject, thus eliminating intergroup variability (as may arise by using NH and HI subjects) at equal SPL as well as equal SL. No differences were observed in gap detection thresholds for both groups at equal SPLs, and better thresholds in hearing impairment at equal SLs were seen in response to the sinusoidal stimulus. On the other hand, findings for the broad band stimulus suggested poorer gap detection thresholds in HI listeners as compared to NH listeners at equal SPLs; at equal SLs, the group difference, although reduced, was still present. Poorer gap thresholds for broadband signals than sinusoidal markers in HI subjects were attributed to greater fluctuations in broadband noise, which may be confused with the gap. Zurek and Formby (1981) found that the change in frequency modulation difference limens (FMDL) in the HI individuals was not attributed to a lack of audibility as measurements were made at 25 dB SL, which was deemed to eliminate level effects. Fitzgibbons and Wightman (1982) examined temporal resolution differences in NH and HI listeners using a gap detection paradigm with octave band noises. Results indicated that the gap detection thresholds of NH subjects were significantly better than HI subjects, both at equal SL and equal SPL, at all the frequencies tested. Since the group differences are evident even at equal SL, the authors concluded that factors other than audibility must account for these observed differences.

Summarily, studies of temporal resolution suggest that at equal SLs, HI listeners have enhanced envelope detection for non-fluctuating stimuli such as sinusoids (Moore &

Glasberg, 1988; Moore, Glasberg, Donaldson, McPherson, & Plack, 1989), but not for stimuli with random amplitude fluctuations (Buus & Florentine,1985; Fitzgibbons Wightman, 1982; Florentine & Buus, 1984; Glasberg, Moore, & Bacon, 1987). However, reductions in envelope detection occur at equal SLs in hearing impairment have been noted even with the use of deterministic stimuli (Jesteadt, Bilger, Green, & Patterson, 1976). Persistence in reduced envelope detection at equal SLs in hearing impairment has been attributed to a combination of inner and outer hair cell loss which can damage both the active mechanism as well as the transduction process (Moore, 1995).

5.1.3 Behavioral studies examining the role of audibility in envelope & TFS cue perception in SNHL

The Articulation Index (AI), a measure of speech intelligibility based on calculations from the long term average speech spectrum and background noise, has been used with varying success to predict speech intelligibility in HI listeners. Dubno & Dirks (1989) used the AI Model at equalized SLs to show that speech perception deficits in hearing impairment were likely due to a loss of audibility, when stimuli were presented in quiet. While the AI has proven to be fairly reliable in predicting speech intelligibility in individuals with mild hearing losses, it has been observed to predict better speech intelligibility than is true in HI listeners with moderate to severe hearing losses (Ching et al., 1998; Pavlovic, Studebaker, & Sherbecoe, 1986; Smoorenburg, 1992). These erroneous predictions based on audibility of the speech spectrum suggest that speech intelligibility in moderate to severe hearing losses depends on more than just access to audibility cues.

Dubno and Schaefer (1992) compared frequency selectivity in NH and HI subjects at equal audibility by using three groups: HI, NH and NH with simulated elevation of thresholds. Simulation of elevated thresholds in NH was achieved using the additive masking technique.. Thresholds obtained in notched noise and broad band noise comprised the measures of frequency selectivity. Findings from this study suggest that frequency selectivity is reduced in HI listeners as compared to NH listeners with simulated elevated thresholds (i.e. even when audibility is controlled). Although the group difference between HI and NH listeners with simulated elevated thresholds (i.e. at equal audibility) is reduced as compared to the group difference between HI and NH listeners when audibility is unadjusted, it still remains a significant difference.

Turner and Robb (1987) studied the role of audibility for differences seen in identification of nonsense syllables between NH and HI listeners. Results from this study indicated that group differences exist at any given presentation level. Additionally nonsense syllable recognition did not reach a 100% even when audibility was maximized to a 100%, providing evidence that factors other than audibility contribute to poor speech perception in moderate to severe hearing impairment.

In general, behavioral studies indicate that speech perception in quiet improves when audibility is restored. However, although differences between NH and HI listeners are reduced at equal audibility, they are not completely eliminated. Restoration of speech perception abilities with access to audibility is also dependent on degree of hearing loss, with greater improvement noted in mild hearing loss as opposed to moderate to severe losses.

5.1.4 Neurophysiological studies examining the role of audibility in envelope & TFS cue encoding in SNHL

Henry et al., (2011) studied the relationship between the auditory brainstem response and single unit measurements from the auditory nerve in chinchillas with noise induced hearing loss. Pre and post noise exposure ABRs were recorded in the chinchillas to tone bursts ranging from 1-8 kHz. Comparisons were made both at equal SPLs as well as equal SLs. The authors found a significant effect of noise exposure for ABR amplitudes at equal SPLs but not at equal SL. Latency values, however, were significantly different (shorter latencies in noise-exposed) at SLs, and to a lesser degree, at equal SPLs. Decrease in ABR latency at equal SL is consistent with a lack of restoration of NH function even after audibility is accounted for.

Wong et al. (1998) compared single unit data in response to a vowel sound in NH and HI cats at three presentation levels. It was observed that phase locking to formant frequencies in NH cats increased as a function of level. In addition, formant capture and synchrony suppression, phenomena where phase locking to formant related harmonics is enhanced and that to non-formant related harmonics diminishes, were observed with increase in level. However, the cats with noise induced hearing loss had significantly reduced/absent synchrony capture.

Woolf et al. (1981) examined neural phase locking at the level of the auditory nerve and cochlear nucleus in chinchillas with NH and ototoxicity induced outer hair cell destruction at multiple presentation levels. Neural phase locking deficits persisted at higher SLs in HI chinchillas where audibility was eliminated as a contributing factor.

5.1.5 FFR studies examining the role of audibility in envelope & TFS cue encoding in SNHL

Plyler and Ananthanarayan (2001) consistently found an effect of hearing loss on subcortical neural encoding of formant transitions (reflected in the spectral FFR) across multiple presentation levels. No improvement in performance of HI subjects was seen when the intensity level was increased from 62 dB SPL to 92 dB SPL. Hence, based on these results, audibility does not restore normal encoding of temporal fine structure cues, and the observed TFS deficit is likely a result of decreased neural phase-locking ability in hearing impairment.

Anderson et al. (2013) studied differences in subcortical envelope and TFS encoding in the FFR obtained to a consonant-vowel /da/ and found enhanced envelope encoding in the HI individuals when the stimulus was adjusted for audibility. Enhanced envelope was attributed to a reduced inhibitory and increased excitatory mechanism. Inconsistent with established perceptual and neurophysiologic literature, no differences were found in absolute TFS encoding of NH and HI individuals. Anderson et al. (2013) underline the need for detailed testing at multiple SPLs and signal-to-noise ratios (SNRs) to confirm these results.

5.2 Rationale

Speech perception and encoding in SNHL is affected by attenuation (lack of audibility) as well as distortion factors. As any incoming signal will undergo attenuation in the HI system, comparisons between NH and HI speech perception and encoding can be confounded when stimuli are presented at the same level for both groups. Findings

from Experiment 1 (described in Chapter 4) suggest that neural phase-locking to both envelope and TFS is degraded in HI; however these results reflect the effects of both attenuation and distortion. Psychophysical, behavioral and neurophysiologic studies reviewed above unanimously agree that there is differential encoding of envelope and TFS information at equal audibility. TFS encoding continues to be degraded in SNHL, even with access to audibility. On the other hand, HI envelope encoding is restored to normal limits or even enhanced in the case of deterministic stimuli (although it may continue to be degraded when there is a combination of IHC and OHC damage). Based on these findings, it may be hypothesized that subcortical neural phase-locking to envelope cues may be enhanced compared to TFS cues at equal audibility levels in SNHL. Specifically, the present experiment aims to characterize level dependent changes in neural encoding of envelope and TFS cues in response to a steady state speech signal in NH and HI individuals using the FFR.

5.3 Methods

Please refer to Chapter 3 (General Methods) for specific details of participant profiles, FFR recording protocols and data analysis techniques.

5.3.1 Participants

- Total number of participants: 20
- NH: 10 participants (male=4, female=6); Age range= 21-32 (M= 24.55; SD=3.35)

- HI: 9 participants (male=6, female=3); Age range= 21-71 (M= 50.66; SD=17.80)

5.3.2 Stimulus

FFRs were recorded to a steady state, synthetically generated, English back vowel /u/ as in WHO'D (F0: 120 Hz, F1: 360 Hz, F2: 970 Hz, F3: 2667 Hz, F4: 3007 Hz;) [as in Experiment 1] at multiple presentation levels ranging between 60-95 dB SPL. The selection of SPLs for each group was based on three factors: the need to collect FFRs for as wide a dynamic range as possible, the fact that a robust FFR is recorded 30-60 dB above the behavioral threshold (Moushegian et al., 1973; Davis & Hirsh, 1976), and the uncomfortable level (UCL) for each participant.

FFRs were recorded at 60, 65, 70, 75 and 85 dB SPL for a subset of 10 NH listeners and at 70, 75, 85, 90 and 95 dB SPL for a subset of 10 HI listeners from Experiment 1. FFRs were collected at these multiple intensity levels to facilitate comparisons at equal SPLs and at equal SLs. In order to compare the NH and HI groups at equal SLs, the audiometric pure tone average at 0.5, 1 and 2 kHz was first computed in dB SPL for each subject in both groups. Next, a simple subtraction procedure (STIM_DBSPL – PTA_DBSPL = SL) determined the SL at which a particular stimulus was perceived for each subject. For e.g. the audiometric pure tone average was 9.5 dB SPL for Subject 4 (NH). Hence, for this subject, a stimulus at intensity 70 dB SPL in the NH group corresponded to 60.5 dB SL. This subtractive procedure was repeated for each subject for each stimulus level in both NH and HI groups. The resultant SLs were averaged to yield a single SL per group per stimulus level. For e.g., the average SL value

for the NH group for a stimulus presented at 70 dB SPL was computed to be 59.60 dB SL. Similarly, at a stimulus intensity of 95 dB SPL in the HI group, the average SL was calculated to be 59.57 dB SL. If the SL value was within 1 dB for the NH and HI, they were considered to be at the same SL, in other words, equally audible. Hence, 70 dB SPL (59.60 dB SL) in the NH group was considered to be at equal in SL (or at equal audibility) to 95 dB SPL (59.57 dB SL) in the HI group.

5.4 Results

5.4.1 Grand averaged FFR waveforms in NH & HI

Grand averages of the FFR waveform for envelope (FFR_{ENV}) and temporal fine structure (FFR_{SPEC}) for the NH and HI groups at different presentation levels are shown in Figure 5.1. As in Experiment 1, NH FFR response waveform amplitude is greater than the HI response waveform amplitude for FFR_{ENV} as well as FFR_{SPEC}, at all presentation levels

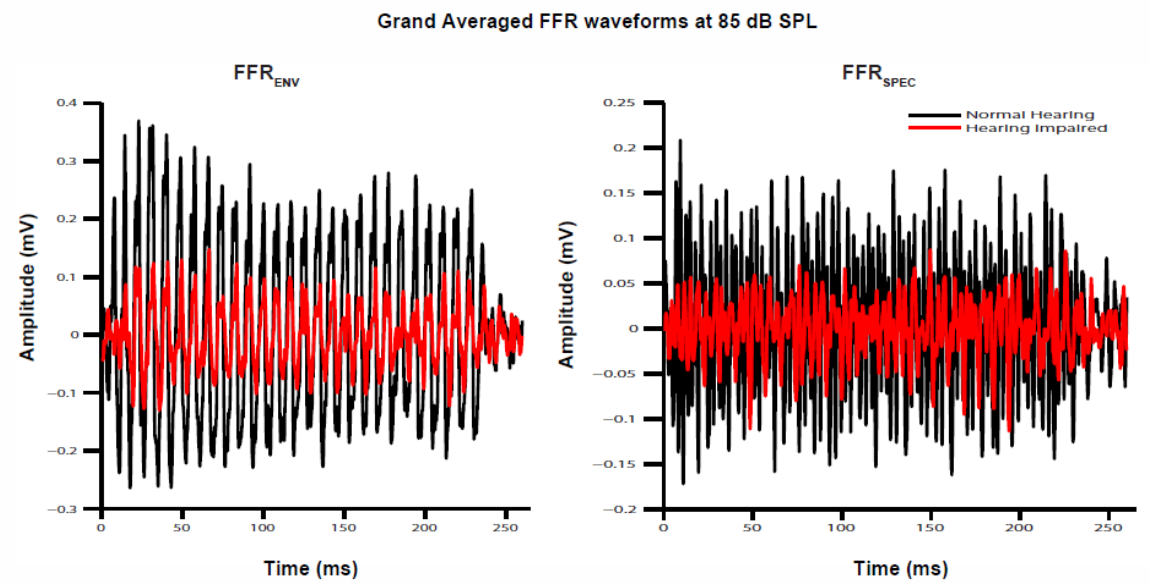

Figure 5.1.: Grand averaged FFR waveforms at 85 dB SPL. FFR grand averaged waveforms for envelope (left) and TFS (right) at 85 dB SPL. HI (red) superimposed on NH (black).

5.4.2 Grand averaged autocorrelograms and spectrograms

Qualitative representations of the group differences in FFR_{ENV} and FFR_{SPEC} at equal SLs are provided in the grand averaged spectrogram and correlogram comparisons. Bands are seen at the F0 (120 Hz) and F1 (360 Hz) in the grand averaged FFR_{ENV} and FFR_{SPEC} spectrograms respectively in both NH and HI. However, the bands in the HI

spectrograms are weaker (lighter) with considerable spectral smearing, as compared to stronger (darker) and precise bands in NH. Similarly, autocorrelograms show stronger (darker) and precise bands are seen at the reciprocal of the F0 in NH subjects, compared to weaker (lighter) and temporally smeared bands in the HI group. Spectral smearing appears to be greater in the FFR_{SPEC} condition as compared to the FFR_{ENV} condition for the HI group. Further, there is a clear improvement in band resolution in the NH group as a function of intensity (dB SPL) which, while present, is reduced in the HI group.

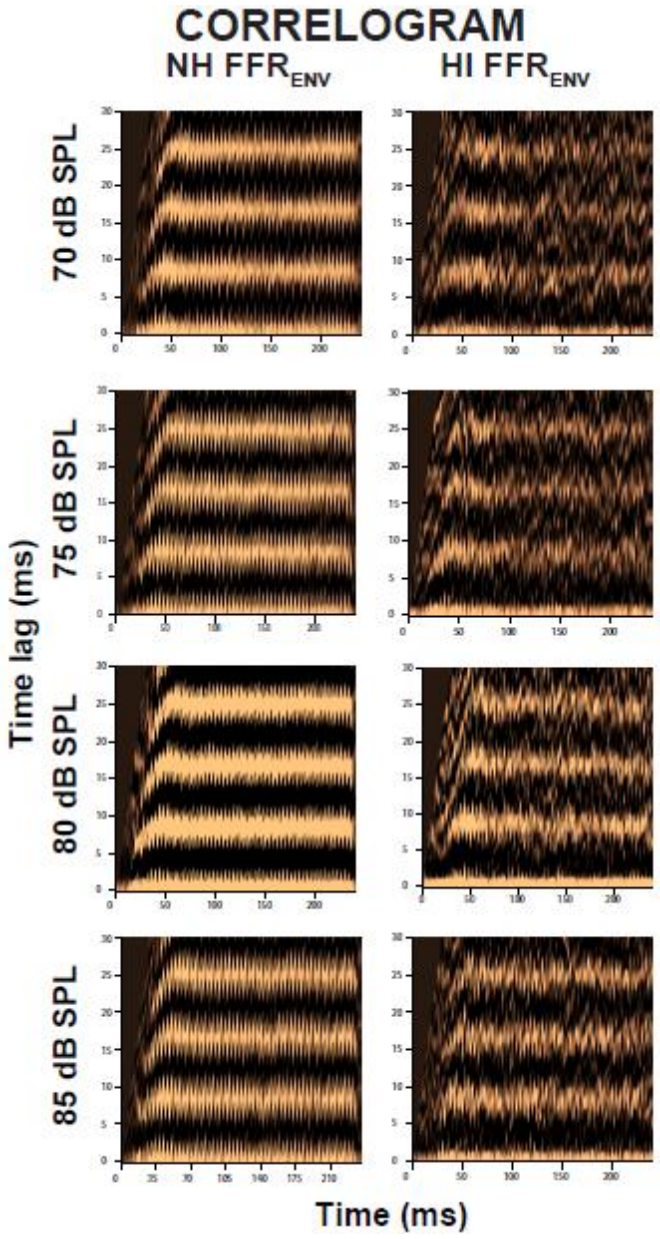

Figure 5.2: Grand averaged correlograms (NH vs. HI) at equal SPLs. Correlograms reflecting FFR envelope encoding (F0=120 Hz, time lag=8ms) in NH (left) and HI (right) at equal SPLs.

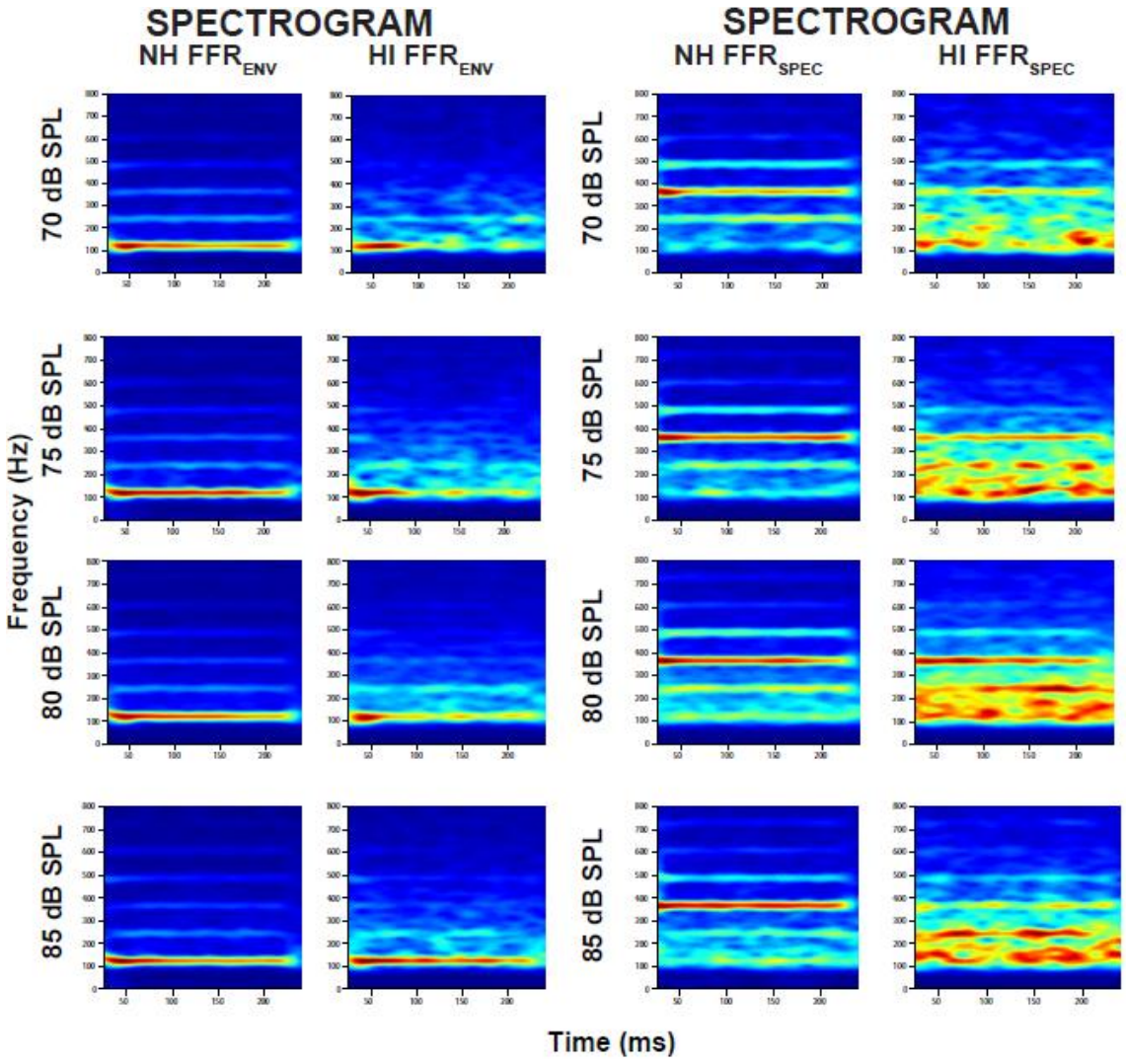

Figure 5.3: Grand averaged spectrograms (NH vs. HI) at equal SPLs. Spectrograms reflecting F0 (120 Hz) (columns 1-2) and formant encoding (F1-related harmonic=360 Hz) (columns 3-4) in NH (left) and HI (right) at equal SPLs.

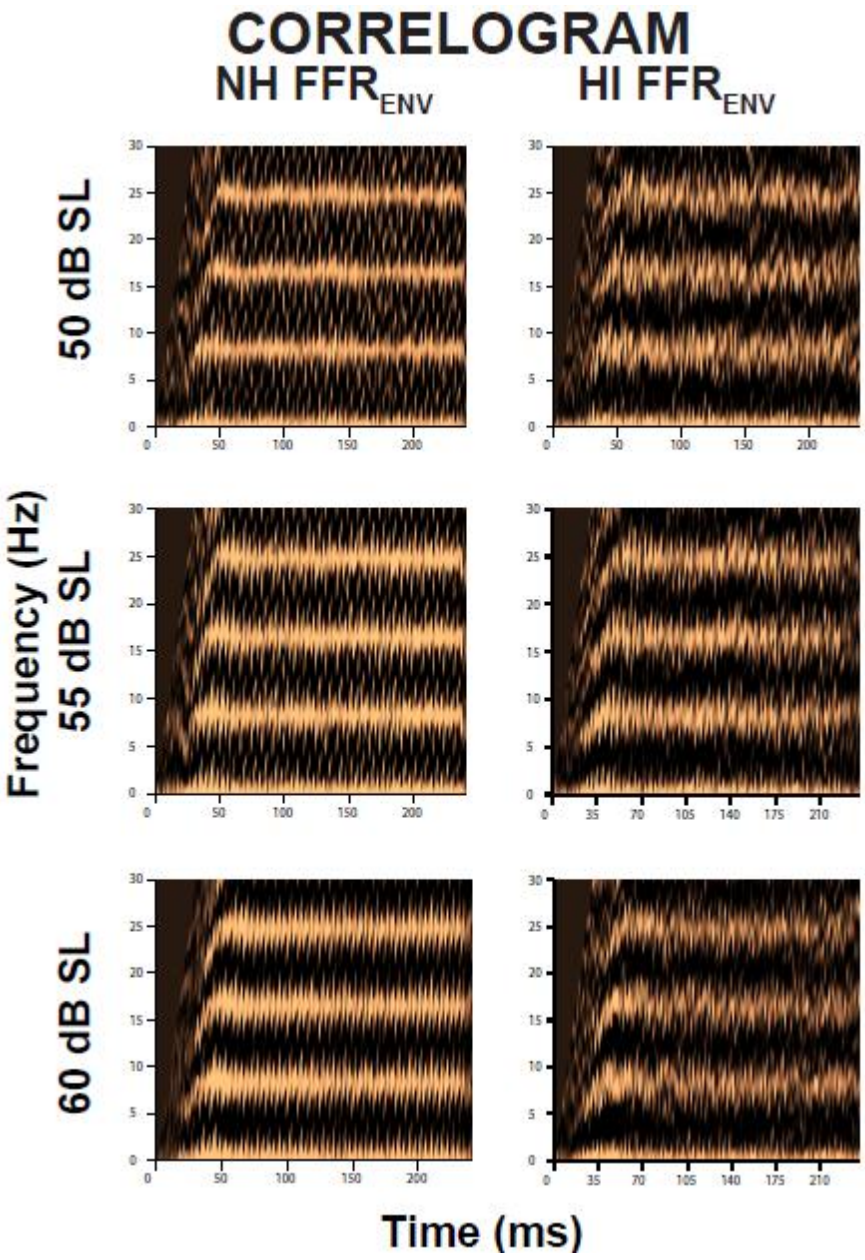

Figure 5.4: Grand averaged correlograms (NH vs. HI) at equal SLs. Correlograms reflecting F0 encoding (F0=120 Hz, time lag=8ms) in NH (left) and HI (right) at equal SLs.

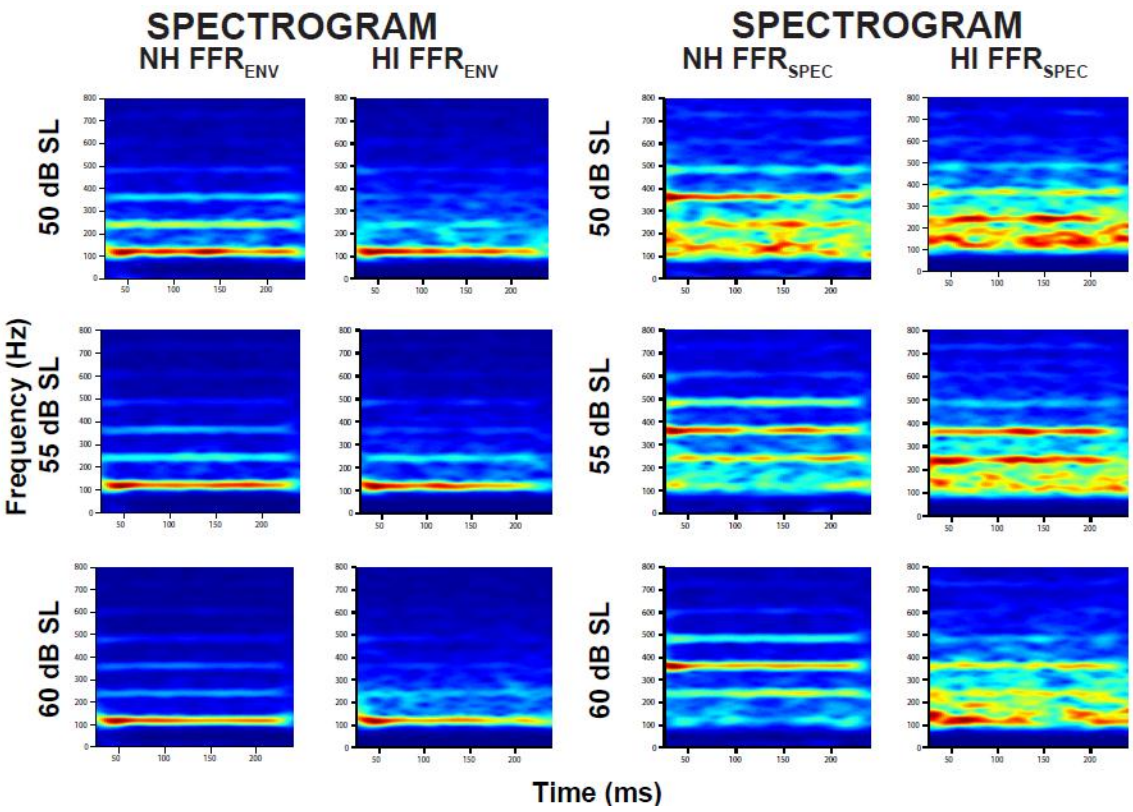

Figure 5.5: Grand averaged spectrograms (NH vs. HI) at equal SLs. Spectrograms reflecting F0 (120 Hz) (columns 1-2) and formant encoding (F1-related harmonic=360 Hz) (columns 3-4) in NH (left) and HI (right) at equal SLs.

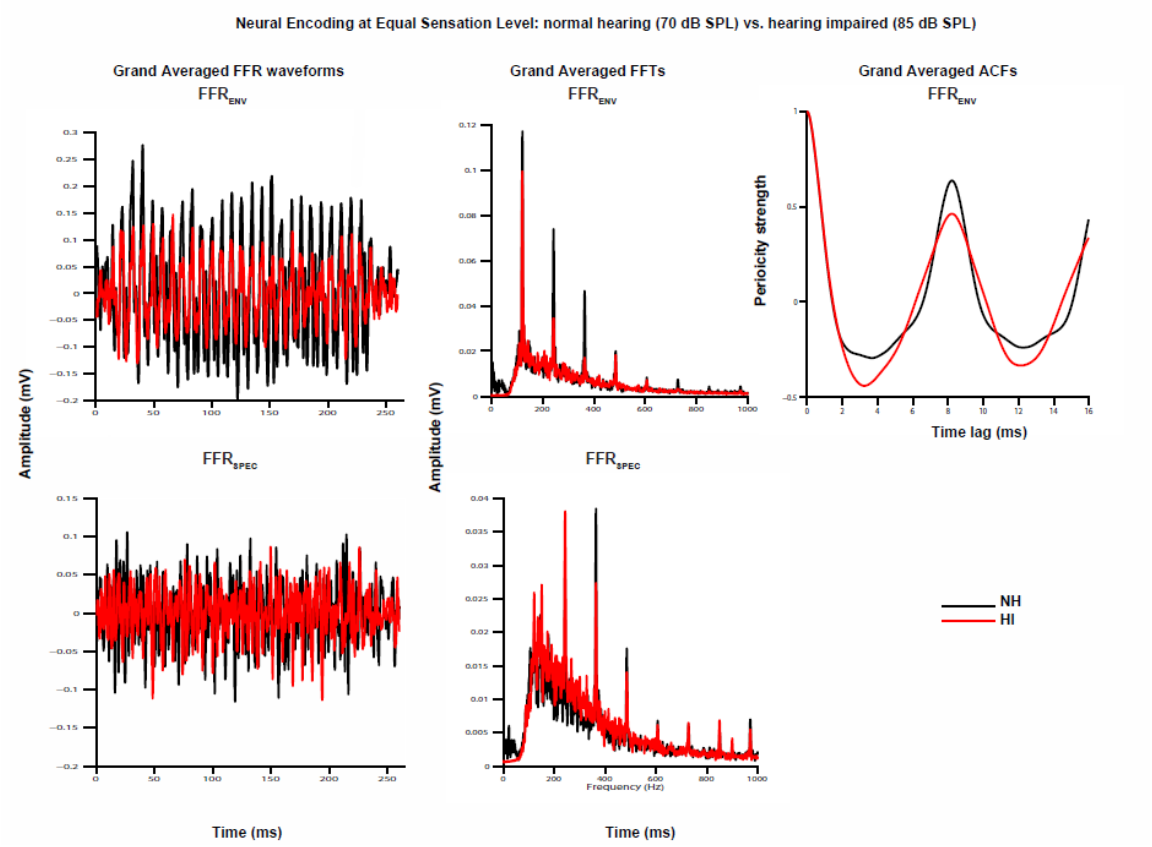

Figure 5.6: Neural encoding in NH & HI at equal SL (50 dB SL): NH (70 dB SPL) vs. HI (85 dB SPL) Grand average waveforms, FFTs and ACFs for NH (black) and HI (red) at equal SL (50 dB SL).

5.4.3 Multiple regression analysis

A multiple regression model, similar to the approach adopted by Henry et al. (2011), was employed to study changes in envelope (F0 magnitude) and TFS (formant-related) encoding as a function of SPL while controlling for the effect of hearing loss. FFT Magnitude of the F0 (or formant related harmonics) was defined as the dependent variable while presentation level (in dB SPL) was the continuous variable, and NH/hearing loss (HL) was the categorical variable.

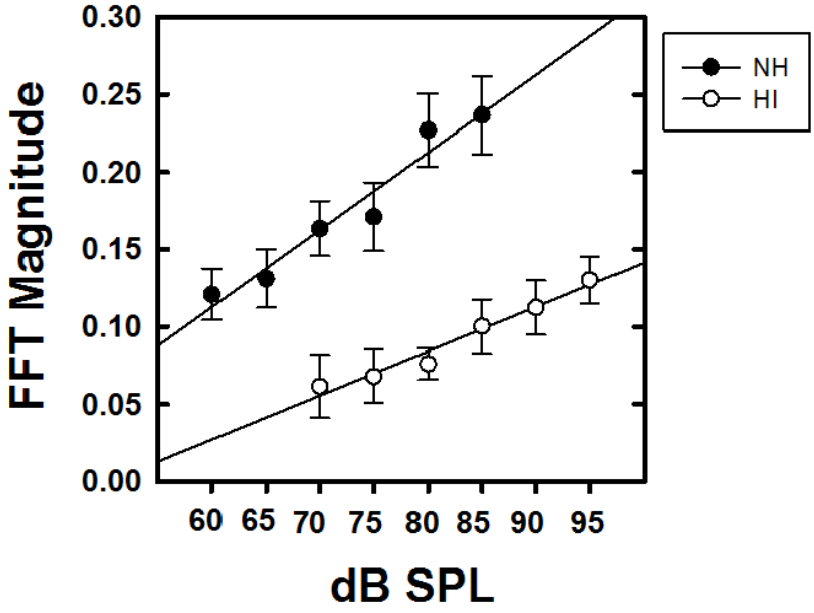

Figure 5.7: Envelope encoding as a function of level (NH vs. HI). Multiple linear regression modeling F0 (120 Hz) magnitudes (FFR envelope encoding) in NH (dark circles) and HI (empty circles) as a function of presentation level (dB SPL).

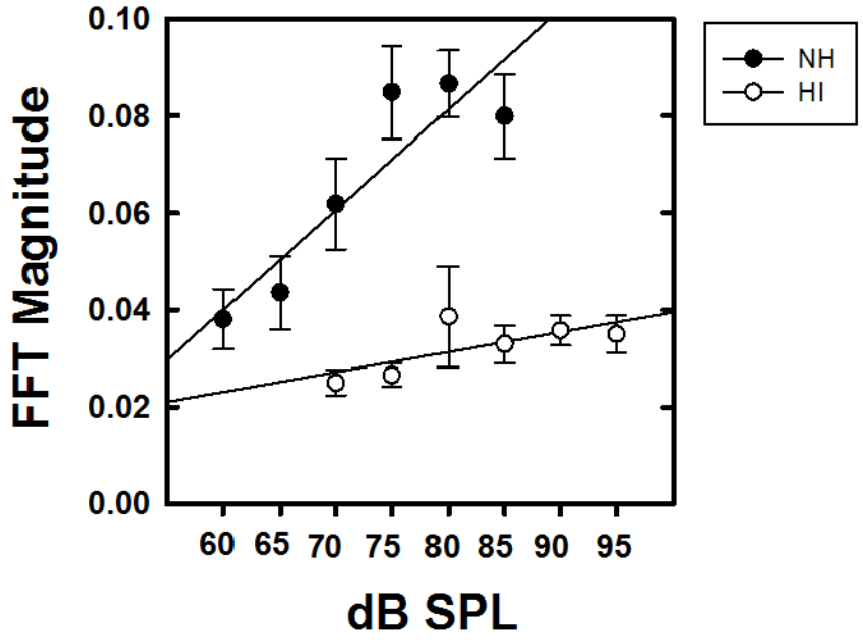

Figure 5.8:TFS encoding as a function of level (NH vs. HI). Multiple linear regression modeling an F1 related harmonic (360 Hz) magnitudes (FFR TFS encoding) in NH (dark circles) and HI (empty circles) as a function of presentation level (dB SPL).

5.4.3.1 FFR_{ENV}

FFR encoding at the fundamental frequency (120 Hz) in both the NH group and HI group shows a significant change as a function of intensity level (NH: t_1 =4.03, p=0.0001; HI: t_1 =4.53, p=0.0001). In other words, as stimulus presentation level goes from the low to high, there is significant increase in envelope encoding in both normal and HI individuals. As a rule, FFR encoding amplitude is greater in NH than HI subjects at all presentation levels, reiterating findings from Experiment 1. Overall, the FFR_{ENV} growth functions for both groups are essentially parallel, indicating no difference in the way envelope information is encoded in NH and HI individuals as a function of intensity.

5.4.3.2 FFR_{SPEC}

Multiple regression models as described in Section 3.3. were also used to examine changes in FFT magnitudes for formant related harmonics at 240, 480, 840 and 960 Hz. Changes in the slope of FFR encoding by intensity level functions were not significant at 240 Hz (t=0.37, P=0.71), 480 Hz (t=1.45, P=0.15), 840 Hz (t=0.77, P=0.44) and 960 Hz (t=-0.12, P=0.902). Identical to the F0 magnitude results, functions representing change in FFR encoding (at these frequencies) across intensity in HI subjects were essentially parallel to the NH functions, albeit shifted to lower magnitudes.

Interestingly, the regression model examining changes in F1 encoding at 360 Hz as a function of intensity level indicates different results. Significant changes in the slope of FFR encoding by intensity level functions were noted at 360 Hz (t= 2.33, P=0.02). In other words, the function representing change in FFR encoding at F1 across intensity in

HI subjects is not parallel to the NH function. As in case of other harmonics, FFR encoding at 360 Hz in the NH and HI group changes significantly as a function of intensity level (NH: t_1 =5.72, p<0.0001; HI: t_1 =2, p=0.04). In other words, as stimulus presentation level goes from the lowest level to the highest level, there is a significant change in TFS encoding in both normal and HI individuals. Again, as in the case of envelope encoding, group differences are preserved at all presentation levels.

5.4.4 Comparisons at equal SPLs & equal SLs

5.4.4.1 Equal SPL

As FFRs were collected at multiple SPLs in both groups, it was possible to compare envelope and TFS encoding at equal SLs and equal SPLs. FFR data was obtained at 70, 75, 80 and 85 dB SPL for both NH & HI. Differences in F0 (envelope encoding) were examined using a two way ANOVA model. The two factors in the two way ANOVA model were hearing loss (2 levels, NH and HI) and presentation level (70, 75, 80, 85 dB SPL in each group). A significant main effect for hearing loss was noted (F(1,67)=71.88, P<0.0001). The main effect for SPL was not significant (F(3,67)=4.05, P=0.01 and neither was the interaction effect between hearing loss and SPL (F(3,67), P=0.91). Bonferroni corrected post hoc multiple comparison testing revealed significantly greater FFR envelope encoding in NH as compared to the HI at all SPLs tested.

The two way ANOVA model used to evaluate F0 encoding was applied to FFR encoding at 360 Hz (the harmonic closest to F1) yielding similar results. A significant main effect for hearing loss (F(1,70)=97.61, P<0.0001). The main effect for SPL was not

significant (F(3,70)=2.2, P=0.09) and neither was the interaction effect between hearing loss and SPL (F(3,70)=0.40, P=0.75). Bonferroni corrected post hoc multiple comparison testing revealed significantly greater FFR spectral encoding in NH as compared to the HI at all SPLs tested.

These results reiterate findings from Experiment # 1, extending the group differences observed at 80 dB SPL to other presentation levels tested in this experiment, namely, 70, 75, 80 and 85 dB SPL.

5.4.4.2 Equal SL

Comparisons at equal SLs were made to determine whether or not audibility causes these group differences observed at any fixed SPL. F0 and F1 measures were compared between NH and HI at the following SLs: 50 dB SL [corresponding to 60 dB SPL (NH) and 85 dB SPL (HI)], 55 dB SL [corresponding to 65 dB SPL (NH) and 90 dB SPL (HI)], and 60 dB SL [corresponding to 70 dB SPL (NH) and 95 dB SPL (HI)].

A two way ANOVA with hearing loss and SL as the two factors and F0 magnitude (envelope encoding) as the dependent variable yielded non-significant main effects of hearing loss (F(1,46)=1.97, P=0.16) and SPL (F(2,46)=2.51, P=0.09) as well as a non-significant interaction effect between hearing loss and SPL (F(2,46)=0.10, P=0.90). Tukey adjusted post hoc multiple comparison testing revealed no significant group differences at 55 and 60 dB SL, but a group difference trending toward significance was observed at 65 dB SL, the highest SL tested.

A similar two way ANOVA model with F1 magnitude (TFS encoding) as the dependent variable yielded a significant main effect for hearing loss ($F(1,46)=4.16$, $P=0.04$) and non-significant main effect for SPL ($F(2,46)=1.74$,$P=0.18$), interaction effect ($F(2,46)=1.21$,$P=0.308$). As for F0 magnitude, Tukey adjusted post hoc multiple comparisons showed no differences in F1 magnitude at 50 and 55 dB SL but a significant group difference was noted at 60 dB SL.

5.4.5 Summary

- Neural encoding of both envelope and TFS cues are reduced in hearing impairment as compared to NH at any given SPL.
- A differential effect of intensity level is noted on envelope and TFS encoding in hearing impairment, with a relative increase in envelope encoding as compared to TFS encoding at higher presentation levels.
- While differences in envelope and TFS encoding between NH and HI are eliminated at 50 and 60 dB SL, group differences continue to persist at 60 dB SL.

5.5 Discussion

FFRs were recorded in response to a steady state vowel /u/ (F0, F1) at multiple SPLs in participants with NH and SNHL. Group differences were noted in both envelope and TFS encoding at equal SPLs (NH > HI), consistent with results from Experiment 1. Increases in neural encoding strength as a function of intensity level were greater for envelope cues as compared to TFS cues, creating a relative deficit for TFS encoding. While group differences between NH and HI were eliminated at lower SLs, neural

representation of speech cues continued to be degraded in HI at the highest SL tested, with a marginal effect for envelope encoding and a significant effect for TFS encoding.

5.5.1 Results supporting the role of audibility

In the present study, group differences were observed only at the highest SL (60 dB SL), which corresponds to 70 dB SPL in NH and 95 dB SPL in HI; these differences were marginal for envelope FFR and strongly significant for the spectral FFR. At lower SLs (50 and 55 dB SL), there was no significant difference between the two groups (although NH participants tended to have stronger neural representation than HI participants as visualized in spectrograms and correlograms). The lack of group differences at 50 and 55 dB SL suggests that envelope and TFS encoding in quiet is equivalent to NH subjects when audibility is restored. This finding is consistent with temporal resolution and speech perception studies that provide behavioral evidence supporting the notion that access to audibility restores normal auditory capacity in HI listeners.

Improved envelope and TFS encoding in HI with increased audibility is supported by findings from speech perception studies. Dubno and Dirks (1989) used the Articulation Index Model at equalized SLs to show that speech perception deficits in hearing impairment were likely due to a loss of audibility, when stimuli were presented in quiet. Speech perception in quiet is not affected in HI listeners as significantly when audibility is restored (Dubno & Schaefer 1992, 1995, Plomp 1978). However, significant differences between NH and HI persist at equal audibility when signals are presented in background noise (Plomp & Mimpen, 1979; Dirks, Morgan & Dubno, 1982). Festen &

Plomp (1983) established correlations between speech perception in quiet and audibility while speech perception in noise was associated with frequency resolution. The stimuli in the current experiment were presented in quiet. Given the established correlations between speech perception in quiet and increased audibility, it may be reasoned that a similar correlation may be partially responsible for the lack of differences between NH and HI for neural envelope and TFS encoding (reflected in the FFR) at lower equal SLs.

Additionally, improvement in speech perception with access to audibility is also dependent on the degree of hearing loss, as demonstrated by various studies using the AI model. In individuals with mild or moderate hearing losses, speech deficits can be explained by the lack of audibility (Ching et al., 1998). All the HI participants in the present study had mild to moderate SNHL, which may also account for the lack of group differences between NH and HI at lower SLs.

Temporal resolution studies (Bacon & Viemester, 1985; Bacon & Gleitmann, 1992; Strickland & Viemester, 1997; Florentine & Buus, 1984) have demonstrated that envelope detection in HI persons is at par with NH persons at equal SLs. Indeed, Moore and Glasberg (1992) found *better* gap detection thresholds in HI subjects at equal SLs for pure tones. Due to loudness recruitment, or abnormal growth of loudness, it is possible that a signal presented at equal SL in a NH ear and a HI ear is perceptually louder in the HI ear, causing improved representation of the signal. This line of reasoning is supported by findings from Wojtczak (1996), who found larger magnitude estimates of AM in impaired hearing as well as Moore et al., (1996) who found that HI ears needed less modulation depth than NH ears to reach the same strength of AM fluctuation. It is

possible that such recruitment based enhancements are responsible for the lack of difference between NH and HI in FFR at equal SL, for FFR_{ENV}.

Findings from Kale and Heinz (2010) show neurophysiologic evidence of enhanced envelope encoding at the level of the auditory nerve in chinchillas with noise induced hearing loss. Kale and Heinz (2010) suggest that envelope enhancement occurs due to steep rate level functions. Rate level functions may be described by C1 and C2 components. C1 components dominate the rate level function at low to moderate intensity levels while C2 components mediate rate level functions at higher intensities (80-90 dB SPL). The high level C2 component is resistant even in moderate to severe SNHL, while C1 responses are eliminated. Steep rate level functions reflective of C2 components in individuals with moderate to severe hearing loss may account for the enhanced envelope effects. Additionally, presence of only C2 responses is correlated with increased inner hair cell loss, while C1 responses were present in HI animals with relatively lesser inner hair cell involvement. Kale & Heinz (2010) infer that envelope enhancement is present to a lesser degree in mild-moderate hearing losses due to loudness recruitment while greater degree of enhancement may be seen in more severe losses due to the involvement of the C2 component. Following this line of thought, the enhancement in envelope encoding noted in the present study may be of a lesser degree as all HI participants had mild-moderate SNHL. This may explain why envelope encoding in HI was equivalent to NH participants, but not enhanced, as has been shown in some gap detection (Moore & Glasberg, 1992) and FFR (Anderson et al., 2013) experiments.

Support for such recruitment based enhanced envelope encoding as described in behavioral and neurophysiologic experiments is present in an analysis of the slopes of the

FFR-intensity functions to envelope and TFS in NH and HI participants. FFR-intensity functions for envelope (F0) and TFS (F1) indicate that the envelope encoding as a function of SPL is similar for both NH and HI, whereas TFS encoding (as represented by the first formant at 360 Hz) as a function of SPL is different. As presentation level increases, envelope encoding increases in a similar manner for both NH and HI. On the other hand, improvement in TFS encoding as a function of presentation level is greater in NH than HI. Put differently, similar improvements as a function of presentation level are noted for neural encoding of both envelope and TFS cues in NH; however, there is a differential effect of improvement (enhancement) with intensity for envelope as compared to TFS encoding for the HI group. These findings suggest a relative deficit in TFS compared to enhanced envelope encoding as a function of presentation level in hearing impairment.

While this interpretation is consistent with perceptual and neurophysiologic data, a cause for concern is the relatively large difference in mean envelope encoding magnitude seen at the highest SL (60 dB SL). Statistically, there is no difference in envelope encoding even at 60 dB SL; however, a closer look at the numbers reveals a trend towards significance. This suggests that such a level dependent improvement may not be sufficient to restore normal neural speech encoding. A number of factors could be responsible for the large difference in envelope encoding seen at the highest SL. The trend towards significance at 60 dB SL may be due to a mere lack of statistical power; in other words, the data set may consist of too few subjects. Another potential reason may be level dependent changes in auditory filters. Additionally, there are persistent

significant differences seen at the highest SL for FFR_{SPEC} that are not explained by loudness recruitment or the balance between C1/C2 components in rate level functions.

5.5.2 Factors other than audibility decide group differences

According to Plomp's dual factor theory of SNHL, effects of SNHL that persist when audibility (attenuation) is accounted for classify as "distortion effects". In general, the clarity of the spectrogram bands corresponding to F0 and F1 in NH, and to some extent in HI subjects, improves with increasing presentation level. However, when spectrograms of NH and HI FFRs are compared at equal SLs, bands in HI subjects continue to show spectral smearing with spurious energy at locations not associated with F0 or formants frequencies. These results are supported by FFR data from Plyler and Ananthanarayan (2001), where the frequency range of a time varying formant represented in the FFR is narrow in NH subjects but much wider in the HI subjects. Persistence of differences between NH and HI at equal SLs suggests that neural phase locking continues to be degraded even when audibility is accounted for. Distortion effects causing degraded phase locking in hearing impairment can include level dependent broadening of auditory filters, impaired phase locking synchrony, reduced frequency selectivity and a decrease in the number of available nerve fibers. Many of these factors were discussed in Chapter 4, but with respect to a single presentation level. Presented below is a discussion of these factors with respect to presentation at equal SLs and SPLs.

5.5.2.1 Level dependent broadening of auditory filters

Level dependent decrease in frequency resolution, compounded by reduced frequency selectivity characterizing SNHL, may partially account for the differences between NH and HI seen in F0 and harmonic encoding at the highest SL, 60 dB SL. Recall that higher presentation levels are associated with broader filters and reduced bandwidths in both healthy and impaired auditory systems. It is plausible that differences between NH and HI are eliminated, or at least reduced, at lower equal SLs in quiet when audibility is restored, but level dependent effects manifest themselves at the highest SL. At 60 dB SL, the presentation SPL is 95 dB SPL in the HI listener as compared to 70 dB SPL in the NH listener. However, the absolute increase in presentation level at 60 dB SL from 50 dB SL is constant for both groups, ~10 dB SPL. According to Ching et al., (1998), speech intelligibility is affected at high presentation levels in both NH and HI individuals to the same extent. Further, according to Moore (2007), level dependent increases in auditory filter bandwidth are reduced in HI as compared to NH. Considering these arguments, level dependent broadening of auditory filters may account for some proportion of the group difference at high SLs; but cannot entirely account for the deficit in HI at these SLs.

5.5.2.2 Impaired temporal mechanisms: Neurophysiologic evidence

A persistent deficit in temporal synchrony with increasing stimulus intensity has been demonstrated by Woolf et al. (1981) in chinchillas with NIHL. No improvements in phase locking were observed at the level of the auditory nerve in HI chinchillas at higher

SLs. Thus, a lack of audibility does not account for the effect of hearing loss, at least as reflected by measures of neural synchrony in the animal model.

The lack of strong formant-related harmonic encoding or "synchrony capture" in the HI FFR has already been discussed in Experiment 1 (Chapter 4). However, this finding was restricted to a fixed intensity level. In the present experiment, the reduction in "synchrony capture" extends across stimulus presentation levels, consistent with findings from Miller et al. (1997). Reduced or absent phase locking to formant related harmonics in hearing impairment at the brainstem level as a function of intensity level has its origins at the level of the auditory nerve. Miller et al. (1997) found enhancement of formant related harmonics ("formant capture") and a reduction the amplitude of components surrounding the formant frequency ("synchrony suppression") in NH cats. Both phenomena were absent in cats with NIHL. Krishnan (2002) found a similar pattern of formant capture and synchrony suppression in the subcortical FFR of NH humans. In the present study, level related changes in the FFR in NH subjects demonstrate an increase in encoding strength of formant related harmonics, consistent with findings from Krishnan (2002).The loss of synchrony capture observed in the HI FFR in the present study suggests reduced precision in subcortical neural phase locking in hearing impairment.

5.5.2.3 Reduced filter selectivity

- Neurophysiologic evidence

Frequency selectivity at high presentation levels continues to be reduced in hearing loss. Evidence from brainstem responses in mice at equal SPLs and SLs supports the notion of reduced frequency selectivity. In electrophysiological work, studies that have used stimuli at equal SPLs in NH and HI (Attias & Pratt, 1984; Nousak & Stapells 2005) have demonstrated increased latency in hearing impairment. At equal SPLs, the HI animals receive the signal at a lower SL than NH animals owing to HI related attenuation. As explained by Henry et al. (2011), lower stimulus levels are associated with an increase in latency, which explains the group differences in latency between NH and HI at equal SPLs.

Further supporting this hypothesis, Henry et al (2011) found significantly different shorter latencies in noise-exposed animals at equal SLs, and to a lesser degree, at equal SPLs. Continuing to find shorter latencies in the noise exposed animals at equal SLs suggests that audibility does not restore NH. Wider than normal auditory filters play a role in deficits observed in hearing impairment even at equal SLs. Latencies are known to increase as intensity level decreases, which accounts for increased latency in hearing impairment at lower SLs. However, a broadening of the usually sharp auditory filters is associated with SNHL-such a broadening will lead to shorter "build-up time" and in turn, reduced latencies.

- Behavioral evidence

Reduction in spectral contrasts between formant peaks and their valleys has been discussed as a possible reason for the lack of formant capture in the FFR of HI listeners (Leek & Summers, 1996; Summers & Leek 1994). Leek & Summers (1996) used

synthetic vowels to determine the role of audibility and frequency selectivity by studying spectral contrast (peak to valley differences) in HI, and NH listeners with masked and unmasked thresholds. While the stimuli in the present study were presented in quiet, Leek and Summers (1996) used a notched noise paradigm when presenting their stimuli. For correct identification of vowels, vowel formant peaks to be at least 1-2 dB above the remaining harmonics for NH listeners, ~4 dB in NH listeners with masking and 7 dB in HI listeners. Differences in audibility between NH and HI were indirectly represented by differences between masked and unmasked responses of NH subjects. Based on this premise, the authors estimated that reduced audibility accounted for about 2-3 dB of the required spectral contrast in HI subjects. The remaining 3 dB difference in required spectral contrast in HI subjects reflects reduced frequency selectivity.

5.5.2.4 Envelope encoding regulated by unresolved regions

Reduced frequency selectivity does not explain the differences between NH and HI given that the stimulus F0 and F1 are relatively low frequencies (120 Hz and 360 Hz) and that average low frequency PTA in the HI subjects in the present experiment is 36.85 dB HL . As in Experiment 1, most of the HI subjects in Experiment 2 had greater high frequency hearing loss (average HF PTA: 43.05 dB HL).

The role of higher unresolved harmonics in neural F0 encoding has been established by neurophysiologic (Cariani & Delgutte, 1996; Meddis & O'Mard, 1997; Sayles & Winter, 2008) as well as neural pitch encoding as indexed by the FFR

(Greenberg et al., 1987;Smalt et al., 2012). It is thought that F0 encoding is determined by phase-locking to modulations produced by unresolved harmonics.

In the case of high frequency hearing impairment, however, poor audiometric thresholds at high frequency regions where unresolved harmonics operate may degrade perception/encoding of the F0. Results from Chapter 4 have demonstrated that phase locking to low frequency stimuli may be degraded even when low frequency hearing is near-normal, but high frequency thresholds are affected. But these results were observed at a fixed intensity level.

A study of gap detection thresholds with changing frequency in NH and HI by Fitzgibbons & Wightman (1982) provides support that these seemingly "remote" effects of high frequency hearing loss do occur even when audibility is accounted for. In addition to an effect of hearing loss for gap detection thresholds at equal SLs, the authors found a frequency dependent change in gap detection thresholds was observed for both NH and HI listeners, with improvements in gap detection with increasing stimulus frequency. Fitzgibbons and Wightman (1982) discuss the possibility that high frequency regions (> 4000 Hz) may play a dominant role in temporal resolution for broad band stimuli. However, listeners with hearing impairment tend to have high frequency hearing loss, while low frequency thresholds may be normal/near-normal. Fitzgibbons and Wightman (1982) hypothesize that reduced frequency selectivity may arise because of deficits in phasic response mechanisms on the basilar membrane. Extending this line of thought to the present data, it is possible that the need for high frequency information for robust temporal resolution combined with reduced high frequency hearing in the HI

listeners may account for the deficits in FFR encoding of at least envelope information with hearing impairment.

5.6 Conclusion

Overall, results from the current experiment suggest that there may be a relative enhancement of envelope encoding over TFS encoding in HI subjects. However, effects of hearing loss are not completely eliminated in envelope encoding with increase in audibility. Access to audibility does not convincingly explain marginal differences in envelope encoding or the robust differences in TFS encoding between NH and HI subjects at high SLs. Based on comparisons with perceptual and single unit studies, persistence of degraded neural phase locking when audibility is restored may be due to impaired temporal synchrony, loss of frequency selectivity and high frequency hearing loss.

These findings become especially relevant in the context of clinical audiology, specifically hearing aid fitting. Enhancement of envelope encoding relative to TFS encoding in SNHL raises interesting questions for hearing aid benefit. Could enhanced envelope encoding result in hearing aid benefit, or will it cause distortions in the amplified signal? More importantly, and perhaps frustratingly, continued effects of hearing loss on TFS encoding despite increased audibility pose challenges for the current amplification technology. While hearing aid technology has vastly improved in recent years, the basic principle still hinges on amplification of the incoming signal, and it has been established by perceptual, physiologic and now subcortical electrophysiology that audibility does not entirely restore normal auditory acuity. Results from the present

experiment are aptly reflected in the most common complaint by hearing aid users and HI individuals: “I can hear you, but I am not able to understand what you are saying”. A better understanding of neural encoding of TFS cues is required to design better signal processing strategies that will someday overcome this current challenge.

CHAPTER 6. EFFECTS OF VARYING STIMULUS CHARACTERISTICS ON SUBCORTICAL NEURAL ENCODING OF ENVELOPE & TFS IN HEARING IMPAIRMENT

6.1 Introduction

6.1.1 Motivation

Effects of hearing impairment on auditory perception and encoding have been established for a range of stimuli (ranging from simple pure tones to complex speech signals) and listening conditions (ranging from quiet to noise and reverberant environments)(Fitzgibbons & Wightman, 1982; Gagné, 1988; B. Moore & Glasberg, 1988; Bacon & Viemester, 1985; Bacon et al., 1998; Baskent, 2006; Buss et al., 2004; Ching et al., 1998; Dubno & Schaefer, 1992; Duquesnoy & Plomp, 1980; Festen & Plomp, 1990; George & Goverts, 2010; Hopkins & Moore, 2011; Hopkins et al., 2008; Buss, & Grose, 2008; Leek & Summers, 1996; Lorenzi et al., 2009; Lorenzi et al., 2006; B. C. J. Moore, 2008; Nábělek & Dagenais, 1986; Nábělek et al., 1996; Nábělek & Robinson, 1982; Nábělek, 1988; Nábělek et al., 1989; Smoorenburg, 1992; Summers & Leek, 1998, 1994). Perceptual deficits in HI listeners have been traced to neurophysiologic changes in the auditory system such as weaker neural phase locking, reduced frequency selectivity, a loss of audibility and impaired temporal synchrony amongst others (Miller et al., 1997; Wong et al., 1998; Woolf et al., 1981).

In addition, behavioral studies have indicated that steady state speech sounds are better perceived than time-varying speech sounds in HI listeners, indicating an effect of pitch contour complexity (Nábělek, 1988). Similarly, neuroimaging (Vouloumanos & Kiehl, 2001) and electrophysiological (Song et al., 2006) studies have documented differences in auditory processing and encoding of speech (vowels) vs. non-speech (complex tones) stimuli in NH. However, the effect of manipulating acoustic characteristics of the stimulus (formant vs. non-formant harmonics, steady state pitch vs. time-varying pitch) on neural encoding of envelope and TFS cues in HI remains largely unexplored, and forms the primary motivation for the present study. A detailed review of behavioral, cortical evoked potential and FFR research documenting the effects of varying stimulus characteristics, mostly in NH listeners, is presented in the following section, forming the basis for the rationale of the current study.

6.1.2 Perception and encoding of "speech" & "non-speech" signals

6.1.2.1 Models of speech perception

Vowels are characterized by a concentration of acoustic energy at specific frequencies known as formants. A vowel is differentiated from a complex tone (with equal amplitude harmonics) of identical duration and F0 by its formant structure. Vowels and complex tones may be classified as "speech" and "non-speech" sounds respectively.

Models of speech perception are divided into two main theoretical stand points with respect to speech processing in the auditory system. According to Diehl and Kluender (1986), speech perception processes are no different from any auditory input,

and employ the same psychophysical mechanisms of detection, discrimination and identification. When a speech signal initially enters the auditory system, it is encoded by parsing together acoustic units that make up the speech sound (Cole & Jakimik, 1980). Pitch features in speech versus non-speech signals as are not subjected to different processing mechanisms, as demonstrated by pitch memory tasks (Semal & Halle, 1996).

On the other hand, Lieberman (1982) and Liberman and Mattingly (1985) propose a modular theory (Fodor, 1983) of speech perception where the auditory system utilizes innate processing mechanisms unique to the speech domain. In other words, the auditory system immediately recognizes and encodes speech input using different mechanisms than non-speech signals. However, Liberman and Mattingly (1988) qualify their modular speech perception theory by suggesting that it is effective only for phonetically relevant features of the speech signal.

6.1.2.2 Neuroimaging studies examining encoding of "speech" & "non-speech" stimuli

Vouloumanos and Kiehl (2001) examined cortical activation in response to speech and non-speech stimuli that were matched spectrally and temporally. The speech stimulus was a monosyllabic nonsense word while the non-speech stimulus was a complex signal comprised of sine wave analogues of the speech sound. The speech sound consistently evoked activation in greater areas and at different locations in the cortex as compared to non-speech sound, consistent with modular theories of speech perception (Liberman, 1996; Fodor, 1983).

Differences in speech and non-speech signal encoding has also been documented by magnetoencephalography (MEG). Stronger MEG responses (indicated by the N100m) were found in response to vowels as compared to tones in the left hemisphere (Gootjes, Raij, Salmelin, & Hari, 1999). Vihla, Lounasmaa and Salmelin (2000) measured MEG responses to vowels and complex tones to study speech vs. non-speech processing at cortical levels using an oddball paradigm and found stronger mismatch fields for complex tones rather than vowels. Using synthetic vowels and consonant-vowels as speech sounds and spectrally-and-temporally matched non-speech analogues, Parviainen, Helenius and Salmelin (2005) demonstrated greater N100m amplitudes in response to speech as compared to non-speech stimuli in the left hemisphere.

6.1.2.3 Subcortical studies examining encoding of "speech" & "non-speech" stimuli

Song et al. (2006) examined the relationship between the click evoked and speech evoked auditory brainstem response in children with learning disability. Comparisons were made between the click evoked ABR and the transient portion of the speech evoked ABR that occur in the first 10 ms post stimulus onset. The authors hypothesized that strong correlations between the two brainstem measures would indicate similar underlying neural processes for speech and non-speech stimuli, whereas absent or weak correlations would suggest different neural encoding processes. ABRs to speech (CV syllable) and non-speech stimuli (clicks) were moderately correlated with each other, suggesting different neural encoding processes for the two stimuli. Per Song et al. (2006), specific neural processing schemes may be responsible for encoding features specific to

speech stimuli such as formant structure. It is possible that the neural processes unique to encoding speech-specific acoustic features may be compromised in impaired populations (e.g. children with learning problems). The authors also suggest that reduced neural synchrony may be a consequence of the longer duration of the speech stimulus vs. the transient click stimulus.

Swaminathan, Krishnan, & Gandour (2008) studied subcortical pitch encoding (as indexed by the FFR) to speech and non-speech stimuli (IRN) in Chinese and English speakers. Findings from this study indicated that brainstem encoding of speech stimuli is greater than that of non-speech stimuli regardless of language group. Thus, the brainstem FFR demonstrates enhanced encoding of signal features that are linguistically relevant.

6.1.3 Perception and encoding of steady & dynamic pitch contours

Speech encoding in the HI system may also be affected by the pitch contour (steady state or time-varying) of the stimulus.

6.1.3.1 Behavioral studies examining encoding of steady & dynamic pitch contours

Time-varying features of speech play a major role in speech identification (Jacobsen et al., 1963). The ability to encode certain time-varying characteristics appears to be affected with hearing impairment. Perception of time-varying pitch cues in diphthongs is affected to a greater extent than speech containing steady state pitch. Nábělek (1988) examined differences between vowel and diphthong perception in reverberation in NH and HI listeners. It was observed that vowel perception is affected to a lesser extent in degraded listening conditions than diphthongs. This may be due to the

robust spectral contrasts at formant frequencies (Leek & Summers, 1987) as well as the steady state nature of the formant frequency (Nábělek & Dagenais, 1986; Nábělek, 1988; Nábělek et al., 1989). Similarly, the second formant transition that provides place of articulation cues for consonants in NH listeners (Liberman, Delatrre, Cooper & Gertsman, 1954; Kewley-Port, 1982) is not successfully utilized by HI listeners with mild to moderate SNHL, leading to causing reduced speech identification scores (Dorman et al., 1985).

6.1.3.2 Subcortical studies examining encoding of steady & dynamic pitch contours

The FFR indexes neural encoding of pitch and spectral information present in speech sounds that have steady state pitch (synthetic vowels) (Krishnan, 2002) as well as time-varying pitch contours (Krishnan et al., 2004; Plyler & Ananthanarayan, 2001; Swaminathan et al., 2008). The FFR is dynamic enough to represent changes in trajectory and direction of pitch, preserving F0 and formant-related information in response to time-varying pitch. A comparison of the various studies investigating subcortical neural encoding to time-varying and time-invariant pitch suggest no obvious advantages for either stimulus in NH participants.

Plyler & Ananthanarayan (2001) found that the ability of HI participants to encode the frequency range of the second formant transition (TFS cue) in stop consonants was significantly reduced as compared to NH participants. The FFR experiment was followed up by a behavioral stop consonant identification task. NH listeners demonstrated better stop consonant identification than HI listeners. Both behavioral and

FFR results indicated that the neural TFS encoding of the HI group was significantly reduced as compared to the NH group. Further, the correspondence between the behavioral and electrophysiological components of the experiment suggests that the FFR is capable of reflecting differences seen at the perceptual level.

6.2 Rationale

The general consensus emergent from behavioral and neurophysiologic studies reviewed above is that envelope and TFS encoding are dependent on stimulus characteristics (pitch contour, formant structure) as well as hearing status (NH vs. HI). The FFR is capable of indexing envelope and TFS cues, in both NH & HI. Hence, it may be reasoned that subcortical neural representations of envelope and TFS are also dependent on the nature of the incoming stimulus. The objective of the present experiment is to investigate subcortical neural encoding in response to stimuli differing in harmonic structure and pitch contour.

6.3 Methods

Please refer to Chapter 3 (General Methods) for specific details of participant profiles, FFR recording protocols and data analysis techniques.

6.3.1 Participants

- Total number of participants: 44 (NH: 25, HI: 19)
- NH:

- Complex tone: 10 participants (male=3, female=7); Age range= 21-27 (M= 23.5; SD=2.22)
- Vowel: 25 participants (male=8, female= 17); Age range: 21-55 years (*M*=27.72 years, *S.D.*=9.33 years
- Diphthong: 15 participants (male=4, female= 11); Age range: 22-32 years (*M*=25.07 years, *S.D.*=2.78 years.

6.3.2 Stimulus

FFRs were recorded to three stimuli in increasing order of complexity:

- Stimulus 1 was a complex tone (F0: 110 Hz, with 15 equal amplitude harmonics) and a duration of 265 ms.
- Stimulus 2 was a steady state, synthetically generated, English back vowel /u/ as in WHO'D (F0: 120 Hz, F1: 360 Hz, F2: 970 Hz, F3: 2667 Hz, F4: 3007 Hz) with a duration of 265 ms.
- Stimulus 3 was a time-varying, synthetically generated diphthong /au/ (F0 ranging from 120-114 Hz, F1 ranging from 680-440 Hz) with a duration of 150 ms.

These three stimuli were selected in order to facilitate comparisons between non-speech and speech sounds, as well as steady state and time-varying sounds for NH and HI listeners. All stimuli were presented at 80 dB SPL in both NH and HI listeners.

6.4 Results

6.4.1 Grand averaged FFR waveforms

Grand averages of the FFR waveform for envelope (FFR_{ENV}) and temporal fine structure (FFR_{SPEC}) for the NH and HI groups are shown in Figure 6.1. As in Chapters 4 and 5, NH FFR response waveform amplitude is greater than the HI response waveform amplitude for both FFR_{ENV} and FFR_{SPEC} across all three stimuli. Thus a more robust neural phase-locking mechanism is seen in the NH group than the HI group no matter the complexity of the stimulus.

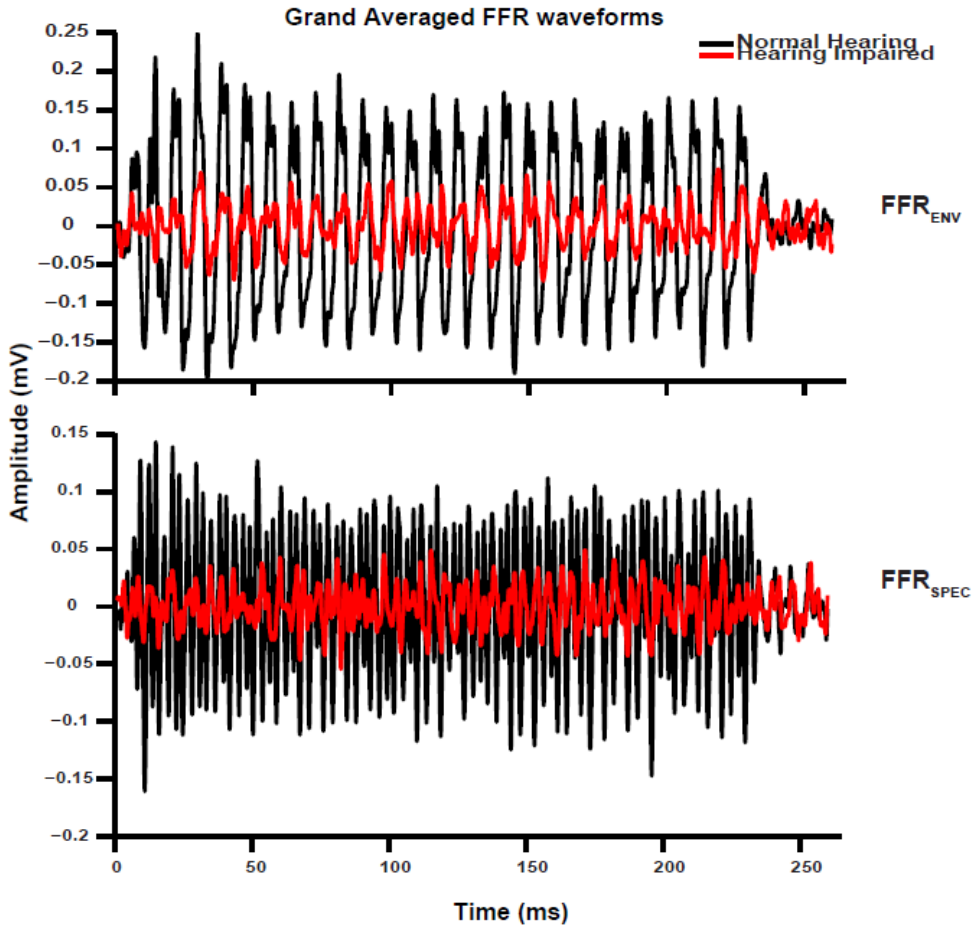

Figure 6.1: Grand averaged FFR waveforms in NH & HI for the vowel /u/. HI responses (red) are superimposed on NH responses (black) for envelope FFRs (top) and spectral FFRs (bottom).

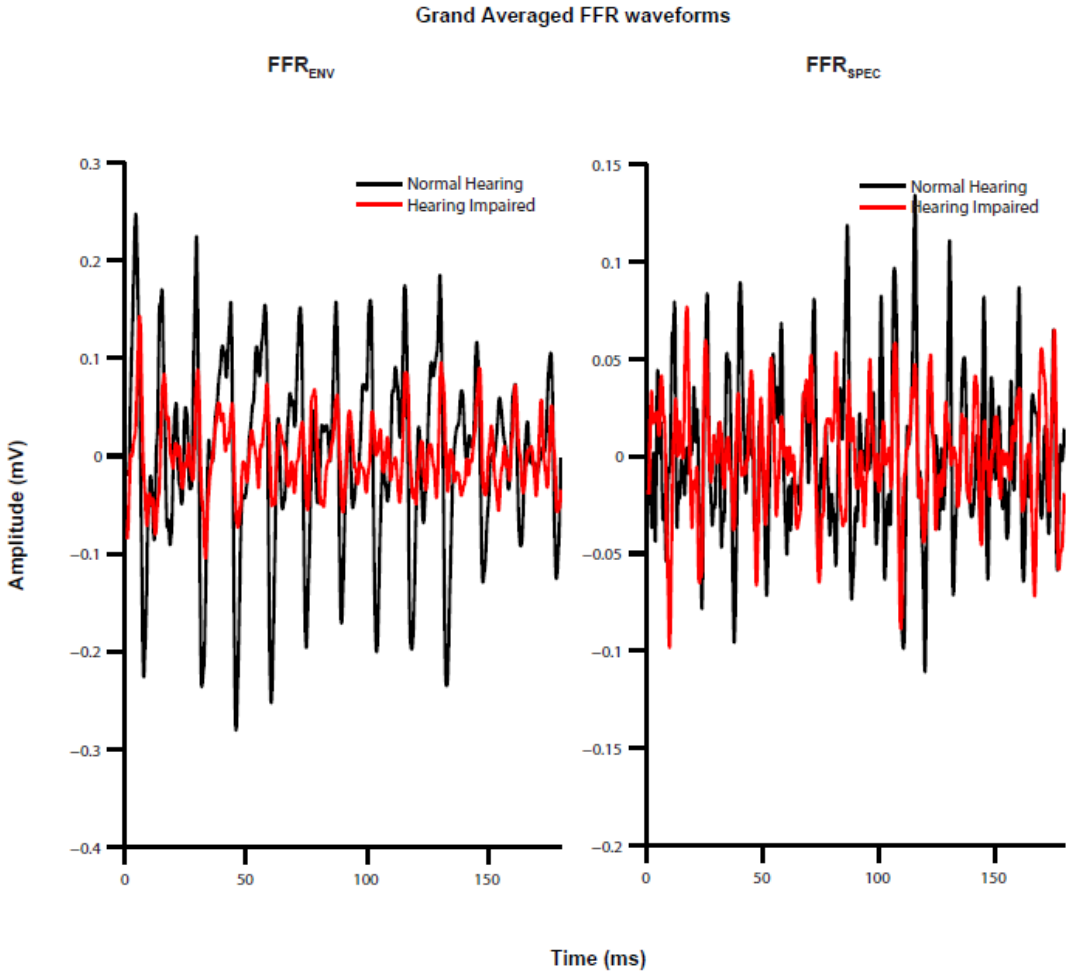

Figure 6.2: Grand averaged FFR waveforms in NH & HI for the diphthong /au/. HI responses (red) are superimposed on NH responses (black) for envelope FFRs (top) and spectral FFRs (bottom).

6.4.2 Grand averaged spectrograms and autocorrelograms

A qualitative representation of the differences between NH and HI for FFR_{ENV} is provided in the grand averaged spectrogram analysis. Stronger and clearer bands of phase locked activity are seen at the F0 in spectrograms of the NH listeners than the HI listeners for all three stimuli. There appears to be considerable spectral smearing in the HI

spectrograms. Further, the spectrogram bands are the most robust for the steady state stimuli as compared to the time-varying stimulus in both NH and HI. Grand averaged spectrograms of the FFR_{SPEC} waveforms for the NH group show a clear band at F1; on the other hand, there is no clear band and considerable spectral smearing in the HI spectrogram.

Reflecting the pitch strength analysis qualitatively, stronger and clearer bands of phase locked activity are seen at the reciprocal of F0 in correlograms of the NH listeners than the HI listeners for all three stimuli. Further, the correlogram bands are the most robust for the steady state stimuli as compared to the time-varying stimulus in both NH and HI listeners.

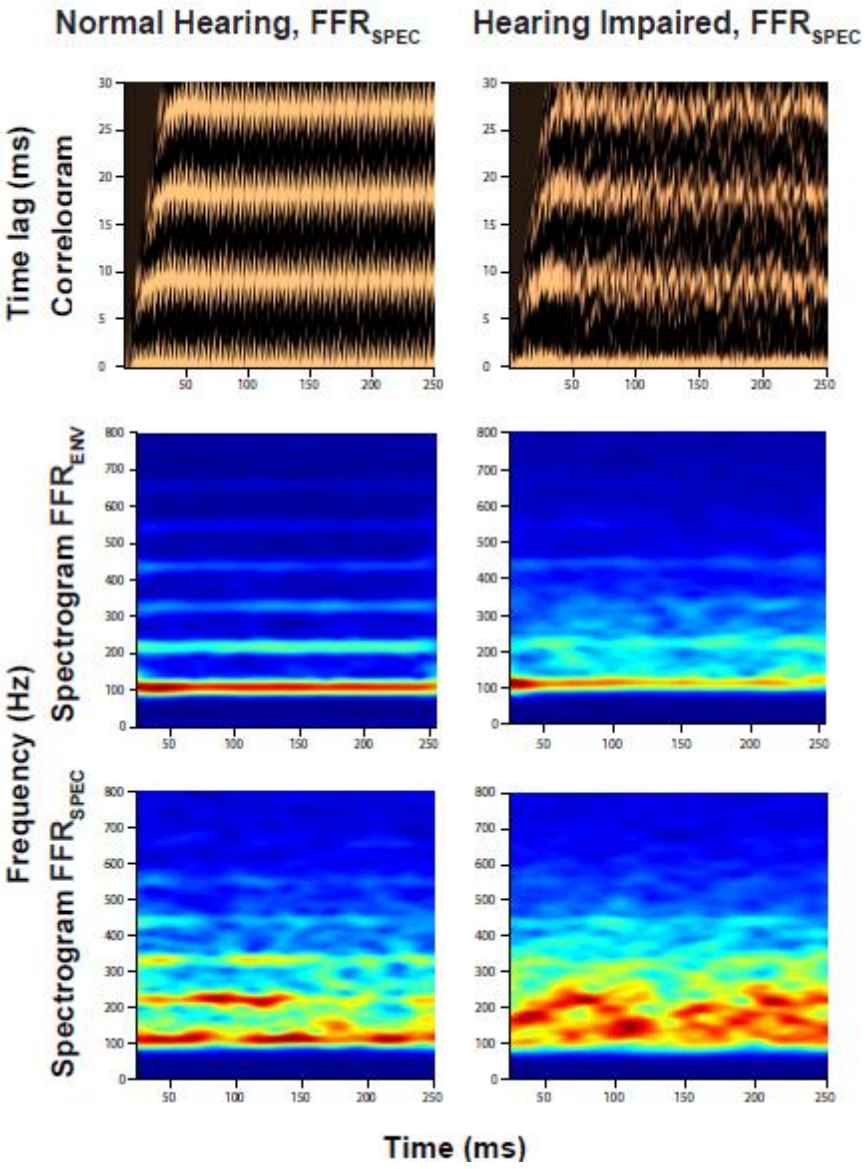

Figure 6.3: Grand averaged autocorrelograms (top) and spectrograms (center and bottom) in NH (left) & HI (right) for the complex tone (F0=110 Hz)

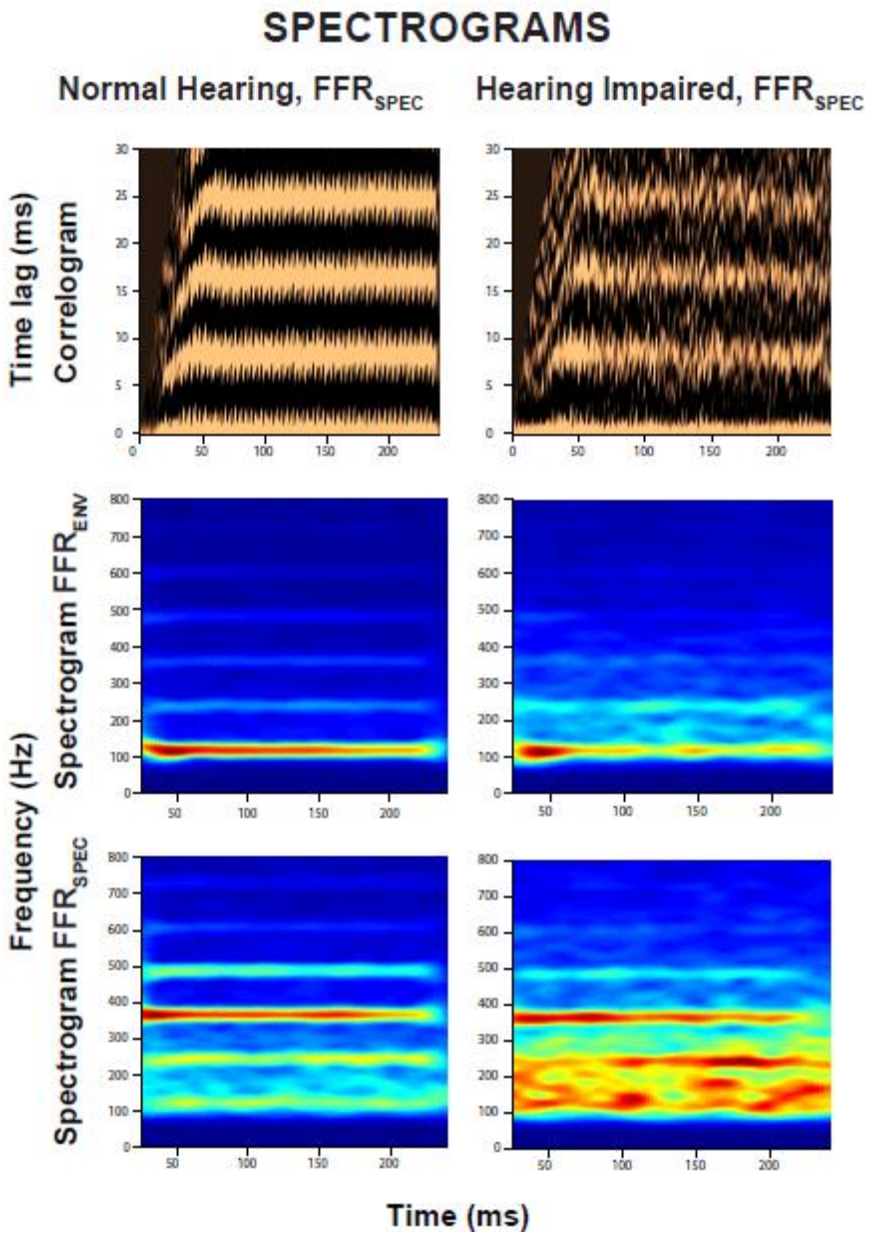

Figure 6.4: Grand averaged autocorrelograms (top) and spectrograms (center and bottom) in NH (left) & HI (right) for the steady state vowel (F0=120 Hz; F1= 360 Hz).

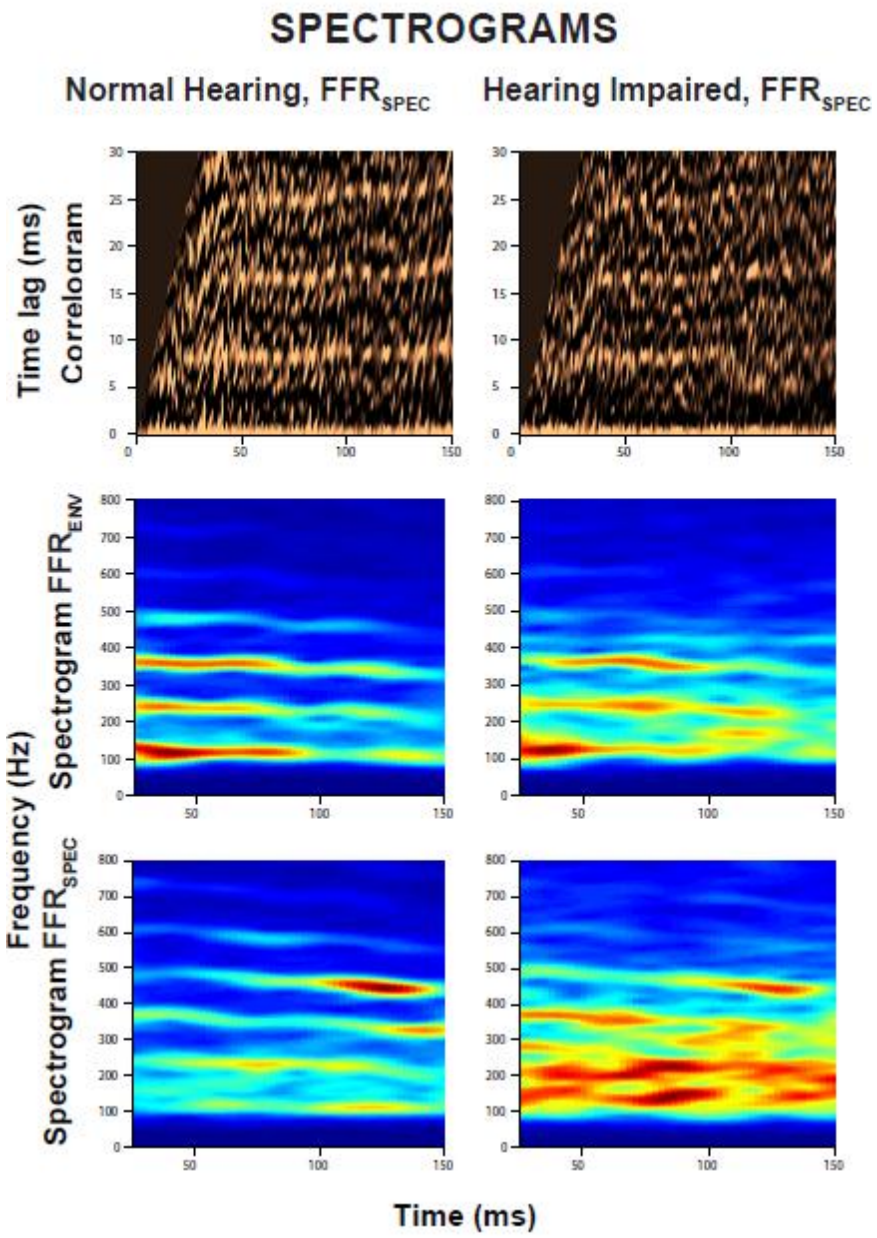

Figure 6.5: Grand averaged autocorrelograms (top) and spectrograms (center and bottom) in NH (left) & HI (right) for the time-varying diphthong (F0=120-114Hz; F1= 680-440 Hz).

6.4.3 Temporal analysis

Estimates of pitch strength or phase-locking to the F0 were obtained for both NH listeners and HI listeners by performing an autocorrelation analysis on the FFR_{ENV}

waveforms for all three stimuli. A two way ANOVA model was used to address the primary question: whether or not group differences are evident between NH and HI listeners with respect to periodicity strength. The two factors in the ANOVA were hearing with two levels (NH and hearing impairment) and stimulus with three levels (steady state non-speech, steady state speech, time-varying speech).

The ANOVA model yielded a significant main effect for hearing loss ($F(1,89)=79.79$, $P<0.0001$), such that pitch strength for NH ($M=0.70$, $S.D.= 0.18$) was higher than the HI pitch strength ($M=0.39$, $S.D.=0.20$). The main effect of stimulus was also significant ($F(1,89)=10.73$, $P<0.0001$)indicating that pitch strength reduces as a function of stimulus complexity. The interaction effect between stimulus and hearing loss was not significant ($F(1,89)=1.03$, $P=0.36$). Grand averaged autocorrelograms of the FFR_{ENV} waveforms for NH and HI for the vowel and diphthong stimuli are shown in Figures 6.6 & 6.7.

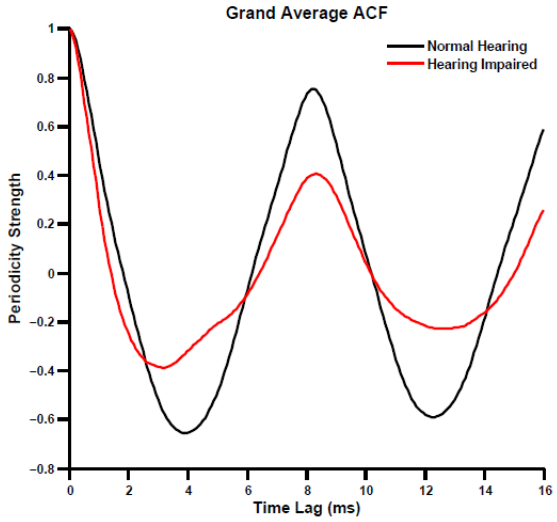

Figure 6.6: Comparisons of grand averaged autocorrelation functions for NH (black) and HI (red) for the vowel /u/

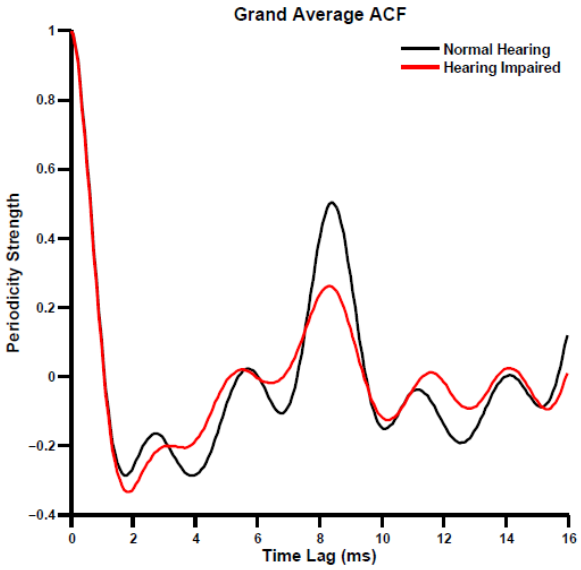

Figure 6.7: Comparisons of grand averaged autocorrelation functions for NH (black) and HI (red) for the diphthong /au/

6.4.4 Spectral Analysis

Grand averaged spectral data of FFR_{ENV} and FFR_{SPEC} reiterates the group differences seen in the waveform data. Robust peaks at stimulus relevant frequencies (F0 and F1) are seen in NH subjects but are reduced in amplitude in the HI group (Figures 6.8 and 6.9).

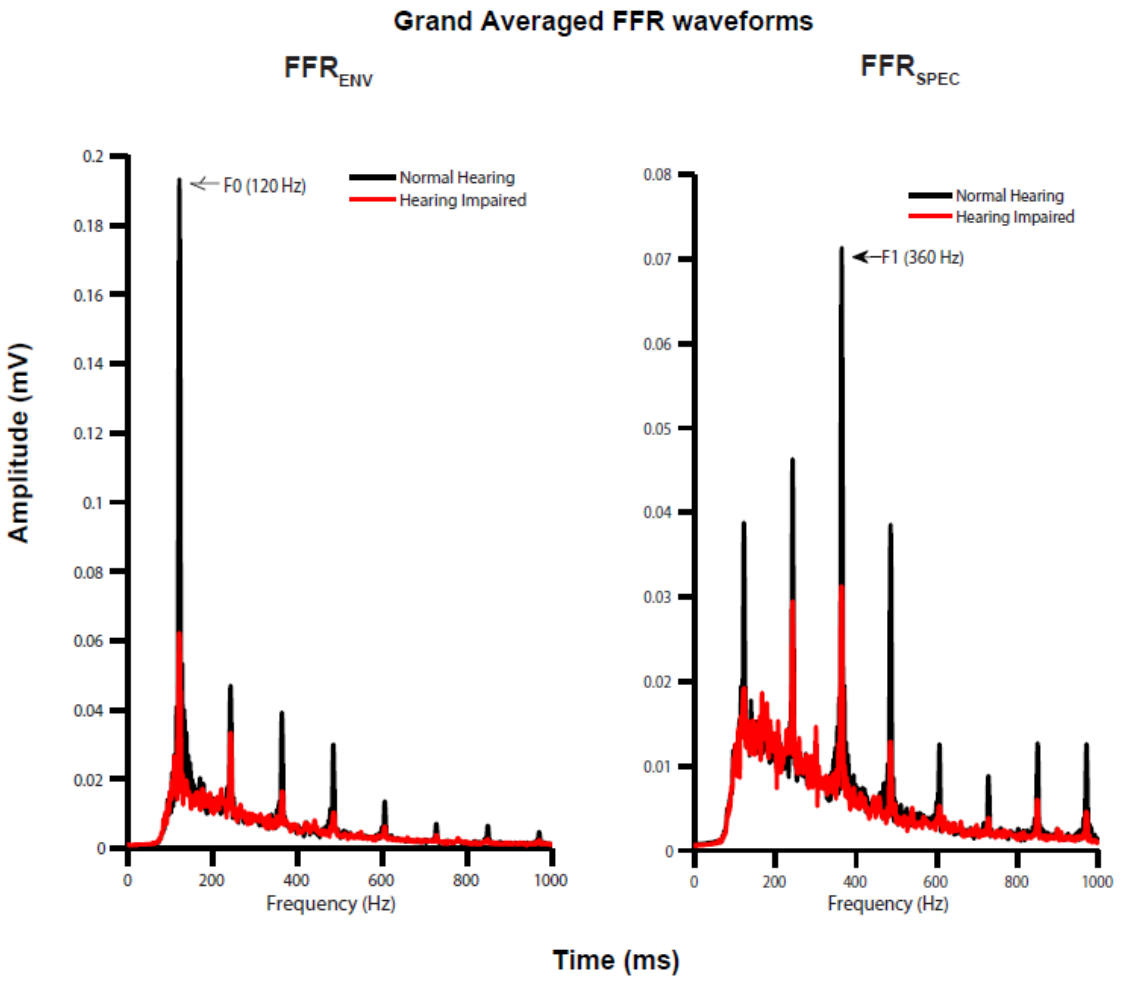

Figure 6.8: Comparisons of FFTs for envelope (left) and spectral (right) FFRs for NH (black) and HI (red) for the vowel /u/

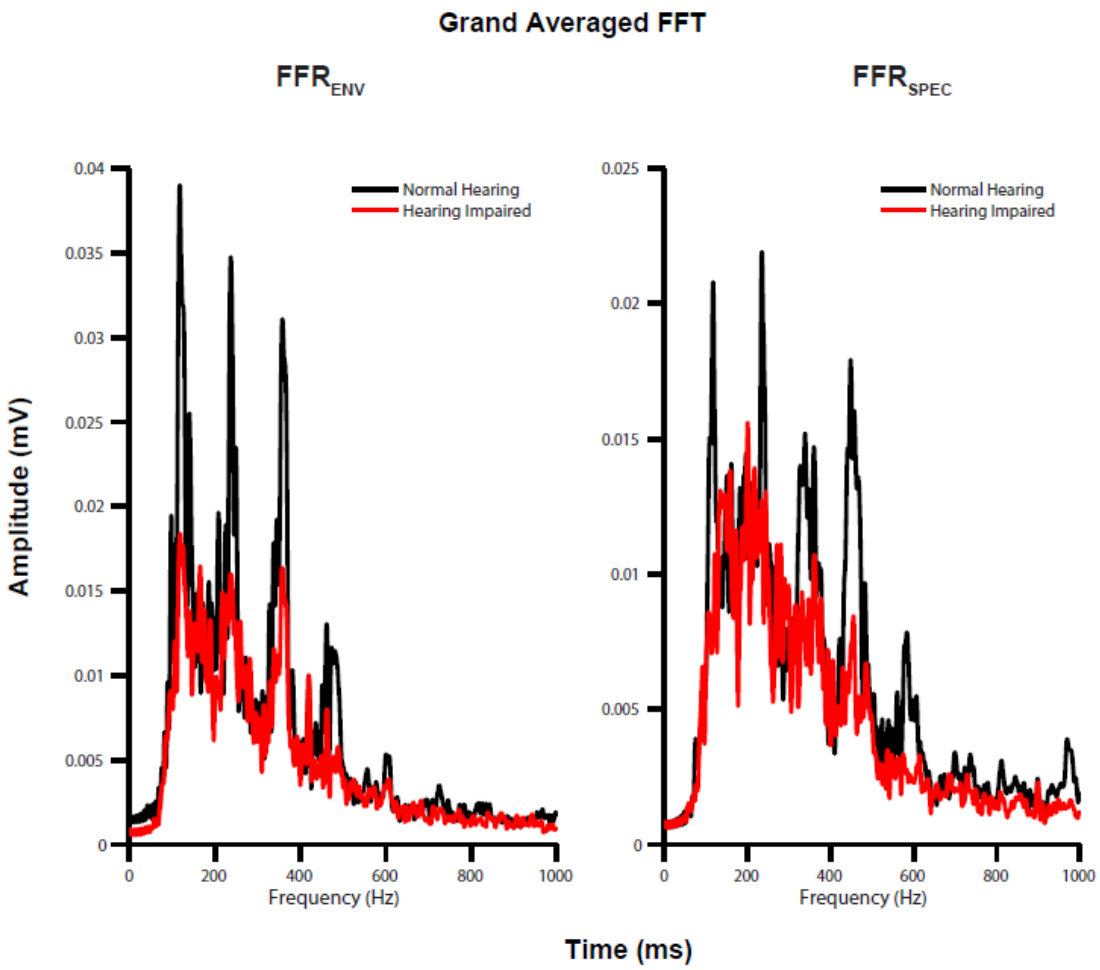

Figure 6.9: Comparisons of FFTs for envelope (left) and spectral (right) FFRs for NH (black) and HI (red) for the diphthong /au/

6.4.5 Statistical Analysis

The absolute magnitude of peak at the F0 was measured in the FFT in the FFR_{ENV} condition to yield a measure of envelope encoding. As in Chapter 5, a natural log transformation on the F0 peak magnitudes in the FFT was required to satisfy model assumptions. A two way ANOVA model was employed to study the effect of stimulus complexity and hearing loss on F0 magnitude. There was a significant main effect for hearing loss ($F(1,88)=57.95$, $P<0.0001$) and stimulus complexity($F(2,88)=65.69$,

P<0.0001); no significant interaction effect (F(2,88)=2.13, P=0.12) was observed. Rerunning the reduced model without the interaction effect yielded significant main effects for both hearing loss (F(1,90)=70.59, P<0.0001) and stimulus complexity (F(1,90)=68.91, P<0.0001).

Magnitudes of the F1-related harmonics in the FFR FFTs were averaged for the vowel (240, 360 and 480 Hz) and diphthong (480 Hz and 600 Hz). Magnitudes at harmonics 220 Hz, 330 Hz and 440 Hz were averaged for the complex tone, corresponding to the F1-related harmonics chosen for the vowel. Once again, to satisfy the assumption for normality required for statistical testing, the harmonic magnitudes were transformed to their natural log form. A two factor ANOVA model was used to analyze the data, with stimulus complexity and hearing loss as the two factors. Statistically significant main effects were obtained for hearing loss (F(1,89)=31.40, P<0.0001), stimulus complexity (F(1,89)=77.90, P<0.0001)as well as the interaction effect (F(1,89)=5.61, P=0.0051). Slicing the interaction effect by hearing loss indicated that a significant effect of stimulus complexity for both NH (F(1,89)=55.97, P<0.0001) and HI (F(1,89)=31.43, P<0.0001) subjects. Slicing the interaction by stimulus revealed an interesting finding: group differences were seen for the steady state vowel (F(1,89)=41.60, P<0.0001) and the diphthong (F(1,89)=12.38, P=0.0007) but not for the complex tone (F(1,89)=0.40, P=0.5287).

Results of two-way ANOVA testing are summarized in Figure 6.10.

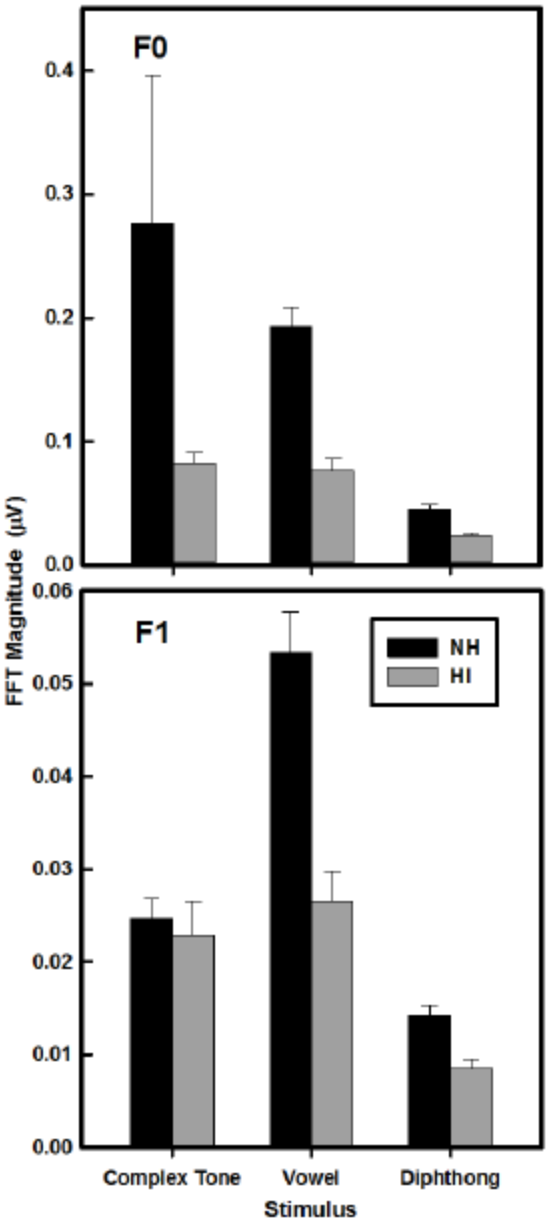

Figure 6.10: Average FFT magnitudes of F0 (top) and F1-related harmonics (bottom) in NH (left) and HI (right) for the complex tone, steady state vowel and diphthong stimuli

6.4.6 Summary

Overall, the results from experiment 3 can be summarized as follows:

- Overall, subcortical neural encoding was more robust in NH than HI subjects for both temporal and spectral based analyses for all three stimuli: complex tone, vowel & diphthong.
- Effects of hearing loss were significant for F1-related encoding for the steady state vowel and diphthong, but not for the complex tone.

6.5 Discussion

Neural encoding of envelope as well as TFS is greater in response to the steady state pitch as compared to the time-varying pitch, in NH and hearing impairment. There are no differences in envelope encoding as stimulus is changed from a non-speech to speech context for both NH and HI subjects. Interestingly, speech- non-speech differences are seen for spectral encoding in NH, but are absent in HI FFRs.

6.5.1 Vowel vs. Complex Tone Encoding

Put together, the results for neural encoding of envelope and TFS cues of speech and non-speech stimuli in NH and HI subjects appear consistent with modular theories of speech perception as proposed by Lieberman and Mattingly (1985). According to the modular theory, while speech perception may be regulated by an innate "speech" mechanism, this is true only for phonetically relevant features of the incoming signal. In the current FFR data, no differences were seen in NH listeners for F0 (envelope) magnitude but a significant difference was observed in encoding of F1-related harmonics (TFS) going from a speech (vowel) to a non-speech (complex tone) context. Both stimuli were very similar in terms of the locations of the F0 (110 Hz in the complex tone, 120 Hz

in the vowel) as well as the harmonics (220, 330, 440 Hz in the complex tone and 240, 360 and 480 Hz in the vowel). However, the harmonics in the complex tone were equal amplitude whereas the selected harmonics in the vowel fell in the first formant region and were hence enhanced in amplitude.

As there are no differences in the representation of the F0 in the complex tone and speech stimuli, it is reasonable to suggest that any differences in the complex tone and vowel likely arise from the harmonic structure. Based on this assumption, FFR encoding of envelope may reflect a more acoustic theory of speech perception, where the F0 magnitude of the complex tone and vowel are processed as acoustic units. This finding, however, is not consistent with FFR work by Swaminathan et al. (2008) who found that periodicity strength (a measure of F0) was stronger in speech as opposed to non-speech contexts in NH. One possible reason confounding the results obtained by Swaminathan et al. (2008) is the use of IRN stimuli for the non-speech context, which contains weak periodicity cues. Neural encoding of TFS, on the other hand, confirms to results from Song et al. (2006) which indicate separate neural processes for non-speech and speech stimuli, as well as the modular theory of speech perception (Liberman & Mattingly, 1984).

Consistent with the NH data as well as the acoustic theory of speech perception, there are no differences in F0 magnitude of speech and non-speech stimuli in the HI FFRs. In other words, the HI system, just like the NH system, treats the incoming complex tone or vowel as a purely auditory signal and does not differentiate based on context. On the other hand, the lack of difference in FFR harmonic encoding suggests a possible interaction between hearing loss and the modular theory of speech perception. Vowel

identification is largely based on formant structure; differences in spectral contrast between formant peaks and troughs provide an important cue for NH listeners in detection and identification tasks. It has also been established through behavioral (Leek & Summers, 1996) and neurophysiologic studies (Miller et al., 1997) as well as findings from Chapters 4 & 5 of this dissertation that there is a loss of spectral contrast and formant capture in hearing impairment, leading to poor encoding of F1-related harmonics in the FFR. It is possible that the lack of differences between speech and non-speech stimuli in HI spectral FFR reflects reduced formant perception and encoding. Hence, the effects of hearing impairment on TFS encoding in speech may eliminate TFS differences in speech – non-speech stimuli within the HI group.

Additionally, envelope encoding appears stronger in NH than in HI FFRs for both speech and non-speech stimuli. Once again, these results are consistent with results from Chapter 4 which show stronger neural encoding in NH for envelope cues for the vowel. Interestingly, the effects of hearing loss are absent for TFS encoding in the non-speech stimulus (complex tone), which is not consistent with established deficits of TFS encoding in hearing impairment. Further systematic investigation of FFRs in response to non-speech stimuli in NH and HI subjects is needed to address this question.

6.5.2 Steady-state vs. Time-varying Stimuli

The other significant result from the current study is that FFR encoding to steady state stimulus was always stronger than to the time-varying stimulus, for both NH and HI subjects. This is consistent with established behavioral literature documenting perceptual advantages for steady state as opposed to time-varying stimuli. Per Walden et al. (1981),

time-varying stop consonants have been found to be more susceptible to the effects of masking and attenuation in hearing loss (Assmann & Summerfield, 2004). More specifically, behavioral studies have observed advantages for vowel over diphthong perception in noise (Nábělek, 1988). Advantages of vowel over diphthong perception have been attributed to steady state pitch in vowels; a similar advantage in neural encoding of the vowel as opposed to the diphthong is observed in the present experiment. However, it is possible that inherently greater spectral contrasts and higher audibility of vowels may also play a role in the observed vowel-diphthong differences. In addition, degradations associated with encoding of time-varying aspects may be superimposed on the effects of hearing impairment in the HI subjects, causing an exacerbation of neural encoding of time-varying speech.

Finally, neural representations of the fundamental frequency as well as formant-related harmonics were stronger in the NH listeners as compared to HI FFRs for both steady state and time-varying stimuli. These results are consistent with FFR findings from Plyler & Ananthanarayan (2001) and data from Chapter 4, as well as established perceptual and physiologic literature. Possible reasons for reduced neural phase-locking in HI subjects in quiet listening conditions at a fixed intensity level could be attributable to impaired neural synchrony, reduced frequency selectivity, aging and loss of audibility. These factors have been addressed in detail in Chapters 4 & 5. Additionally, the effects of aging must be considered. Parthasarathy and Bartlett (2011) found significant differences in AMFRs and FMFRs in young and old rats at reduced modulation depths and complex envelope shapes. These differences were not seen when the modulation depth was high or the envelope was unaltered, suggesting that temporal processing is more susceptible to

age effects when the stimuli are complex. Therefore, the effects of age cannot be ruled out in the present study where stimulus complexity is increasing in a way from steady state to time-varying pitch.

6.6 Conclusions

Overall, findings from this study indicate that differences in stimulus context and complexity seen at the behavioral level are translated to subcortical representations as well. In terms of clinical implications, these results suggest that use of the FFR as a clinical tool in audiological (re) habilitation may be optimized by using ecologically relevant speech stimuli that are relatively simple in terms of acoustic structure. Of course, speech in everyday life is time-varying rather than steady-state and the results from the present study demonstrate that the FFR can be successfully recorded to a time-varying stimulus in HI listeners. However, the FFR may not index further variations in stimulus complexity with the precision required in clinical testing. Hence, results from this experiment suggest opting for relatively simple stimuli to optimize FFR representations in hearing impairment.

CHAPTER 7. EFFECTS OF BACKGROUND NOISE ON SUBCORTICAL NEURAL ENCODING OF ENVELOPE & TFS CUES IN HEARING IMPAIRMENT

7.1 Introduction

7.1.1 Motivation

Everyday speech communication rarely occurs in quiet laboratory conditions or in a sound treated booth. Adverse listening conditions constantly tax the auditory system and the processes responsible for speech extraction from the background noise. Speech perception deficits in individuals with SNHL are usually exacerbated in degraded listening conditions such as listening in background noise. According to Plomp and Duquesnoy (1982), SNHL is determined by two major factors: "attenuation" and "distortion". Attenuation refers to the reduction in audibility, while distortion is speech deficit that remains after audibility is restored (Leek & Mollis, 2009; Plomp & Duquesnoy, 1982). Distortion effects cause a "reduction in the functional SNR" (Plomp, 1978), affecting speech-in-noise understanding even in mild SNHL (Plomp, 1978; Plomp & Mimpen, 1979; Plomp & Duquesnoy, 1982). Per Plomp and Duquesnoy (1982), attenuation plays a greater role than distortion for speech understanding in quiet for HI listeners. However, in degraded listening conditions, speech perception is predominantly determined by the distortion component. Many perceptual studies (Plomp, 1978; Dubno, Dirks, & Morgan, 1984; Nábělek & Dagenais, 1986; Nábělek et al., 1996; Nábělek, 1988) have examined speech sound identification and discrimination in background noise in

hearing impairment. Neurophysiological findings by Henry and Heinz (2012) demonstrated that envelope encoding is enhanced while TFS encoding is drastically affected in background noise in HI chinchillas. These results form the primary motivation underlying the current experiment, which examines subcortical representations of envelope & TFS in noise in the normal and impaired auditory systems. The following section describes perceptual and neurophysiological literature on envelope and TFS perception/encoding in hearing impairment, as well as experiments that use the FFR to study the effects of SNR on signal encoding in NH participants.

7.1.2 Behavioral studies examining envelope & TFS cue perception in background noise

7.1.2.1 F0-based source segregation in competing backgrounds

F0 plays an important role in speech-in-noise perception, which is mediated by speaker identification and object formation (Oxenham, 2008; Shin-Cunningham & Best, 2008). Findings from Brokz and Nooteboom (1982), and Bird and Darwin (1988) suggest that listeners tend to group together similar components in the auditory signal, i.e. components that arise from the same source (same F0). Stream segregation, or the ability to separate sounds that arise from different channels (different F0), can be achieved through simultaneous or sequential grouping (Oxenham, 2008). Simultaneous grouping based on F0 is evident in tasks involving concurrent vowel identification (Assmann & Summerfield, 1987).

F0-based simultaneous segregation is reduced in hearing impairment (Summers & Leek, 1998). Summers and Leek (1998) measured F0 discrimination abilities of NH and HI listeners for synthetic vowels presented in isolation and concurrently. This was followed by a sentence recognition task. For F0 DL with isolated vowels, no effect of hearing impairment was observed; in fact, several of the HI listeners performed within the range for NH listeners. Performance on the concurrent vowel task was strongly correlated with performance on the single vowel task. Hence, poor F0 discrimination is associated with reduced ability to segregate competing signals in hearing impairment. However, F0 discrimination abilities did not directly predict sentence recognition, which was also influenced by the effects of aging.

7.1.2.2 Formant perception in noise

Acoustic energy at harmonics close to the first three formants are usually enhanced in the vowel spectrum, which creates a typical signature for each vowel. Formant frequencies shaping the speech spectrum creating “spectral peaks” provide the listener with phonetic information that aids in vowel identification. These spectral peaks become essential cues especially when listening in background noise or when frequency resolution is degraded (Assmann & Summerfield, 1989). Formant-related spectral speaks can be altered in the presence of background noise. According to Roberts and Moore (1990, 1991) competing sounds such as narrowband noise in the F1 region of a vowel has an impact on the amplitudes of resolved harmonics as well as the phonetic quality of the vowel. Altered phonetic quality possibly occurs because of the addition of extra

components (competing signal) that interferes with the spectral signature of the original signal (Roberts & Moore, 1990, 1991). In NH listeners, perceptual grouping mechanisms differentiate the target signal from competing signals by eliminating inharmonic components that are time asynchronous with remaining harmonics in the vowel (Darwin 1984; Roberts & Moore, 1990, 1991). A harmonic sieve analysis (Duifhuis, 1982) that operates by including only F0-related harmonics may underlie grouping mechanisms that analyze the formant-related harmonic structure of vowels (Roberts & Moore, 1991). However this analysis technique is inadequate when discrimination of concurrent vowels with differing F0s is concerned. Autocorrelogram approaches based on temporal pitch extraction theory suggest that autocorrelation functions are constructed at every frequency channel, and then grouped together based on common F0s.

Time-varying formant transitions are more susceptible to the effects of background noise as compared to steady-state vowels. Since these transitory segments (such as those observed in stop consonants) are shorter in duration and lower in amplitude, they are more easily masked by noise (Miller & Nicely, 1955). Further, they are also vulnerable to attenuation and masking effects seen in hearing loss (Walden et al. 1981).

7.1.2.3 Type of background noise

Multitalker babble is considered representative of everyday noisy listening conditions (Duquesnoy 1983, Festen & Plomp, 1990). Multi-talker babble can alter spectrum shape as well as reduce the spectral contrasts, although low frequency

harmonicity is still preserved. The first and second formants are often still resolved even at a SNR of 0 dB, although there is a reduction in the peak-to-valley difference in magnitude at these locations. Bacon et al. (1998) compared the speech recognition performance of NH and HI listeners using different kinds of background noise, and found that steady-state speech shaped noise (used in the present experiment) has similar effects on speech recognition as multitalker babble.

Loss of spectral contrast poses challenges for HI individuals, who lack the fine frequency resolution (Simpson, Moore, & Glasberg, 1990; Baer, Moore & Gatehouse, 1993) needed to detect the reduced spectral contrasts. The importance of spectral contrast in vowel perception has been further demonstrated by Plomp and Mimpen (1979), who showed that spectral smearing reduced vowel identification. While the amount of reduction of spectral contrast is not related to measures of frequency selectivity (Keurs, Festen, & Plomp (1993), increasing spectral contrast for formants in individuals with SNHL improves speech recognition to a certain extent, suggesting a partial effect of audibility (Baer et al., 1993).

7.1.2.4 Behavioral studies of vowel & diphthong perception

Nábělek and colleagues conducted a series of studies (Nábělek & Dagenais, 1986; Nábělek et al., 1996; Nábělek, 1988) on vowel and diphthong identification in degraded listening conditions such as background noise and reverberation in HI listeners. Nábělek & Dagenais (1986) studied identification of fifteen English monophthongs and diphthongs (including /u/ and /au/ which are used in the present experiment) in quiet and

noise in ten subjects with SNHL. The noise condition used a multitalker babble as the masker. Results showed a significant effect of listening condition, indicating that the performance of the HI subjects in quiet was significantly greater than their performance in the noise condition. Nabalek and Dagenais (1986) suggested that vowel confusion errors in noise in HI listeners may be related to an inability to resolve formant frequencies that are located close spectrally in the confused pair. Similarly, diphthongs presented in noise were most commonly mis-identified as their beginning monophthongs. Diphthongs contain time-varying formant transitions; Nabalek and Dagenais (1986) found that the formant frequency in the initial segment of the diphthong was similar to the formant frequency in the monophthong they were mis-identified as. These results indicate poor frequency selectivity in hearing impairment

In 1988, Nábělek studied the contributions of age and hearing loss to vowel identification in quiet, noise and reverberation. Of relevance for the current experiment are the results obtained for the quiet and noise conditions. Results indicated that there was a strong correlation between hearing loss (indexed by three different pure tone averages) and vowel identification overall; the correlation was greater for degraded listening conditions than in quiet. In other words, hearing loss was a better predictor of vowel identification in noise or reverberation than in quiet.

Leek and Summers (1996) investigated the effects of decreased frequency selectivity in vowel perception in noise in NH and HI listeners. Spectral contrast, or the difference between peaks and valleys of formant frequencies and auditory filter bandwidths was measured in both groups. Results indicated that greater spectral contrasts are required by the HI subjects who have reduced frequency selectivity as indexed by

wider auditory filters at 2 kHz. The authors suggested that reduced SNRs at the outputs of wider than normal auditory filters in HI listeners could contribute towards reduced vowel perception in noise.

Leek and Summers (1996) further determined the roles of audibility and frequency selectivity in vowel perception by studying spectral contrasts in HI and NH listeners with masked and unmasked thresholds. The authors employed a notched noise paradigm during stimulus presentation. For correct identification of vowels, vowel formant peaks were found to be at least 1-2 dB above the remaining harmonics for NH listeners, ~4 dB in NH listeners with masking and 7 dB in HI listeners. Differences in audibility between NH and HI were represented by differences between masked and unmasked responses of NH subjects. Based on this premise, the authors estimated that reduced audibility accounted for about 2-3 dB of the required spectral contrast in HI subjects. The remaining 3 dB difference in required spectral contrast in HI subjects reflects reduced frequency selectivity.

Nábělek (1995) found that level of the F2 transition relative to the level of the noise and overall level of the stimulus determined diphthong identification in noise. For example, HI listeners were able to correctly identify the diphthong /ai/ when the F2 transition was 21 dB lower than the maximum stimulus level; however, when the S/N was 0 dB, the level of the F2 transition had to be no more than 11 dB lower than the maximum stimulus level.

Findings from behavioral studies suggest that vowel perception in background noise is affected due to a loss in spectral contrast. These effects are exacerbated in

individuals with hearing impairment who lack the fine frequency resolution power needed to separate reduced spectral contrasts in noise.

7.1.3 Neurophysiologic studies examining envelope & TFS cue perception in background noise

Differences in neural encoding of envelope and TFS in quiet listening conditions at the single unit level have been well documented (Miller et al., 1997; Woolf et al., 1981; Kale & Heinz, 2010). Recent work by Henry & Heinz (2012) has shed new light on envelope and TFS encoding in the presence of background noise. Henry & Heinz (2012) recorded single unit responses from chinchillas with NIHL to broadband stimuli presented in background noise. They found that while envelope encoding remains enhanced, significant deficits are observed in TFS encoding in the HI animals.

Hearing loss can cause downward shifts in frequency tuning of TFS encoding in the CFs of auditory nerve fibers, which may have specific implications for hearing in noise. Phase-locking in the auditory nerve fibers tuned to CFs < 4 kHz encodes both envelope and TFS information (Recio-Spinoso, Temchin, van Dijk, Fan & Ruggero, 2005). As phase-locking decreases with increasing frequency, higher CF fibers mainly encode envelope information. A downward shift of frequency tuning of TFS and envelope encoding was observed in chinchillas with NIHL, such that high CF units that normally encode envelope information were observed to encode low frequency TFS information (Henry et al., 2012). Such a shift in the CFs has implications with respect to degraded speech perception in noise for listeners with hearing loss. It is possible that high frequency information in speech, which would normally be encoded by high frequency

CFs is represented by fibers with lower CFs. Additionally, background noise which is typically low frequency in nature, is also encoded by the same low CF fibers, leading to degraded speech perception.

7.1.4 Effects of aging on envelope & TFS perception & encoding

Effects of aging on speech perception and encoding in NH and HI listeners using behavioral, electrophysiological and neurophysiologic experiments have been extensively by Gordon-Salant (2005), and Pichora-Fuller and Singh (2006) [as well as in Chapter 9]. In general, effects of aging on signal perception are not usually evident in quiet environments with adequate audibility, but manifest themselves in complex auditory tasks (e.g. gap detection) and in challenging listening situations such as reverberation and background noise. In addition, a variety of stimulus factors influence the results, including but not restricted to type of speech signal, masking noise, SNR and hearing impairment.

Dubno and Dirks (1984) found significant differences in speech recognition scores between young and old adults (matched for audiometric thresholds) when background noise was introduced, but not in quiet. These age effects persisted in both NH and HI groups, suggesting that speech understanding in background noise is not a sole function of audiometric threshold, but also age. Nábělek (1988) found that overall vowel identification was correlated with age, however, closer inspection revealed that correlations with age were observed only for the degraded listening conditions.

Parthasarathy, Cunningham & Bartlett (2010) examined AMFRs in response to SAM tones in quiet, noise and at different presentation levels collected from ten young

and ten aged rats. No age effects were noted in the TMTF obtained in response to stimuli in quiet. On the other hand, significant group differences were noted in the TMTFs in the presence of background noise, suggesting age effects are present in AMFR encoding in degraded listening conditions. The authors suggested that these results may be related to reduced inhibitory mechanisms in the aging auditory system.

Frisina and Frisina (1997) conducted a study on speech recognition in noise in young and old adults with NH as well as older HI adults, in order to better understand the neural mechanisms underlying presbycusis. Stimuli included spondees, sentences with contextual cues to identify the target word and sentences without contextual cues to identify the target word, presented in quiet and in multi-talker babble. Many notable findings emerged from the study, including the effect of age and, the effect of hearing loss and the combined effect of age and hearing loss. It was observed that old NH subjects performed on par with young NH subjects in quiet, but the NH young subjects had a significant advantage when background noise was introduced. Thus, an age effect was observed when listening in background noise. Additionally there were no differences between the speech-in-noise recognition abilities of NH and HI listeners (young and old) for spondees and sentences with contextual cues. However, when contextual cues were absent, speech recognition scores were significantly improved as a function of age (young>old) and hearing (old NH > old HI). Based on these findings, cortical contributions from the speech/language area toward the deficit in speech-in-noise understanding were ruled out, as both the older NH and HI participants utilized contextual cues in sentence recognition to their advantage. The authors reasoned that differences between NH and HI could be due to a combination of peripheral effects and

central nervous system changes, likely occurring in the auditory brainstem or auditory cortex.

7.1.5 Electrophysiologic (FFR) studies examining envelope & TFS cue perception in background noise

The effects of SNR on neural encoding of auditory signals has been investigated at the subcortical level. Brainstem response latencies to clicks and pure tone stimuli are delayed at lower SNRs (Ananthanarayan & Durrant, 1992). Li & Jeng (2011) studied noise tolerance in subcortical pitch processing by examining SNR effects on neural phase-locking to speech. Their question was motivated by findings from speech perception studies which indicate that pitch perception occurs at SNR conditions as unfavorable as -10 dB, demonstrating adaptation effects to the noise. Li and Jeng collected FFRs from NH Chinese subjects in response to a time-varying Mandarin syllable /yi/ presented at three intensity levels, with SNR levels varying from clean to -12 dB. The noise presented was a Gaussian broadband noise. Significant effects of both SNR and stimulus intensity were noted on the FFR. SNR effects were observed at around 0 dB or lower, suggesting that neural pitch representations in NH listeners are fairly robust to the effects of background noise.

Several studies report on changes in subcortical neural representation of speech-in-noise in NH participants and groups with language-based learning impairments or reduced speech perception scores (Anderson, Skoe, Chandrasekaran, Zecker, & Kraus, 2010; Cunningham et al., 2001; Parbery-Clark et al., 2009; Russo et al., 2005). Anderson et al. (2010) examined subcortical neural correlates of speech-in-noise perception in

children with high and low speech-in-noise scores. Magnitudes of F0 and the second harmonic in the FFR obtained to a consonant vowel /da/ were compared with scores from the Hearing In Noise Test (HINT). Results suggest that neural encoding of the F0 and second harmonic is significantly reduced in children with poor speech-in-noise scores. Based on these results, the authors conclude that neural pitch encoding of time-varying speech may be a strong predictor of speech-in-noise performance.

Russo (2004) found a significant effect of noise on neural speech encoding of the CV syllable /da/ in NH subjects. F0 and F1 amplitudes, as well as stimulus-response correlations, were reduced in the noise condition. Onset peaks in many subjects were indiscernible due to background noise. Overall, however, the neural encoding in noise, although reduced as compared to neural encoding in quiet, was relatively intact. A point of interest was that F0 encoding was more resistant to effects of noise as compared to F1 encoding-perhaps indicating that envelope encoding is not as susceptible to degradation as TFS encoding.

Cunningham et al. (2001) compared subcortical and cortical responses to a speech sound in quiet and background noise in normal children and children with learning problems. The primary focus of this study was to characterize deficits in children with learning problems, and it was established that LP children had reduced neural encoding of speech-in-noise as compared to normal children. Although this result was not explored further, the authors established a difference between the quiet and noise conditions for the NH subjects in at least one section of the neural response.

Parberry-Clark et al. (2009) compared neural encoding of speech in quiet and in noise from musicians and non-musicians, hypothesizing that experience dependent

learning effects would result in stronger neural encoding in noise for musicians. The stimulus was a speech sound /da/, which was presented at a +10 dB SNR with speech babble in the noise condition. Results showed a significant effect of noise and group for stimulus-response correlations and magnitude of harmonics. Further investigation revealed that there were no group differences in quiet, but significant differences were present in S-R correlations as well as the harmonic structure in the noise condition. Interestingly, there was no main effect for noise or group on F0 magnitude (envelope related cues). Although the main focus of this study was on differences between musicians and non-musicians, it is of note that stimuli presented in background noise caused degraded neural phase-locking in NH non-musicians.

Finally, Anderson et al. (2013) examined the roles of envelope and TFS encoding as reflected by the FFR in NH and HI listeners in quiet and noise. Envelope encoding was enhanced in the HI listeners in noise, while TFS encoding was unaffected. However, enhancement of envelope in background noise produced a relative deficit in TFS encoding in the HI subjects. Anderson et al. (2013) suggest that enhanced envelope encoding may be a result of reduced inhibition and increased excitation in the HI system, or as a consequence of broader filters. However, no satisfactory explanation is available for the lack of absolute TFS deficit, which is contradictory to established behavioral and neurophysiologic literature.

7.2 Rationale

Listeners with hearing impairment face significant challenges in background noise. The general consensus emerging from a review of these behavioral and

neurophysiologic studies is that both envelope and TFS cue perception and encoding are significantly affected in the presence of background noise in hearing impairment. Additionally, FFR studies in NH subjects have shown that subcortical neural representations of speech are degraded in the presence of background noise, with a differential effect on envelope and TFS encoding. However, the effects of background noise on envelope and TFS encoding in HI system remain largely unexplored. Anderson et al. (2013) stress the need to evaluate neural TFS encoding at multiple SNR levels. The aim of the present experiment is to offer a systematic evaluation of neural envelope and TFS encoding at varying SNRs for steady-state and time-varying speech stimuli.

7.3 Methods

Please refer to Chapter 3 (General Methods) for specific details of participant profiles, FFR recording protocols and data analysis techniques.

7.3.1 Participants

- Total number of participants: 39 (NH=20, HI=19)
- In "clean" condition:
    - NH: 20 participants (male=7, female= 13); Age range: 21-55 years (*M*=36.14 years, *S.D.*=13.7 years)
    - HI: 19 participants (male=8, female= 17); Age range: 21-89 years (*M*=54.26 years, *S.D.*=19.40 years)\
- At +5 and -5 dB SNR:

- NH: 9 participants (male=2, female=7); Age range= 22-27 (M= 24.33; SD=1.87)
- HI: 9 participants (male=5, female=4); Age range= 22-72 (M= 52.77; SD=15.86)

.

7.3.2 Stimuli

FFRs were recorded in NH & HI subjects to two stimuli at three different SNR conditions:

- Stimulus 1 was a steady state, synthetically generated, English back vowel /u/ as in WHO'D (F0: 120 Hz, F1: 360 Hz, F2: 970 Hz, F3: 2667 Hz, F4: 3007 Hz) with a duration of 265 ms.
- Stimulus 2 was a time-varying, synthetically generated diphthong /au/ (F0 ranging from 120-114 Hz, F1 ranging from 680-440 Hz) with a duration of 150 ms.

Both stimuli were presented at 80 dB SPL in a "clean" condition (no noise), +5 dB SNR and -5 dB SNR conditions. Speech-shaped noise was used as the background noise.

The electrophysiological FFR data was supplemented by a behavioral speech perception task in order to compare and contrast brain-behavior performances in the presence of background noise. The speech perception task, using test material from the Hearing In Noise Test (HINT), was administered to a subset of the NH and HI subjects who took part in the electrophysiological FFR study. The HINT, developed by Nilsson, Soli & Sullivan (1994), is a test of speech perception in the presence of speech shaped white noise. The protocol followed in the present study reflects only a portion of the extensive HINT administration protocol, and was designed to reflect as closely as

possible the stimulus presentation paradigm in the electrophysiological task, while still using clinical test material.

Most comfortable levels (MCLs) were determined in sound-field prior to administering the HINT for all participants. During the HINT,HI participants were positioned at a 0 degree angle from the speaker closest to their better ear (right ear for NH)and at an angle of 90 degrees from the speaker closest to their poorer ear (left ear for NH). Participants were seated at a distance of 1m from the speakers. Participants were required to repeat short semantically and syntactically simple sentences spoken by a male (e.g. "The boy ran down the path"). Target sentences were presented from the speaker located at 0 degrees while speech shaped noise was presented from the speaker located at 90 degrees. The presentation level for the target sentences was fixed at the MCL while the level of speech-shaped noise was varied. Two lists consisting of 10 sentences each were administered at each of the following conditions: "clean" (no noise), +10, +5, 0 and -5 dB SNR. Performance at each listening condition was quantified by the percentage of words repeated correctly per list.

7.4 Results

7.4.1 . Grand averaged FFR waveforms in NH & HI

Grand averages of the FFR waveform for envelope (FFR_{ENV}) and TFS (FFR_{SPEC}) for the NH and HI groups for different SNR levels for the vowel /u/ and the diphthong /au/ are shown in Figure 7.1-7.4. NH FFR response waveform amplitude is overall greater than the HI response waveform amplitude for both FFR_{ENV} and FFR_{SPEC} for all but the most unfavorable SNR condition (-5 dB), indicating a more robust neural phase-

locking mechanism in the NH group than the HI group. In addition, it can be observed that in the NH group, the FFR waveform becomes more robust as a function of SNR; i.e. the response amplitude is larger at the +5 SNR condition as compared to the -5 condition. Such an effect is not seen in the HI group.

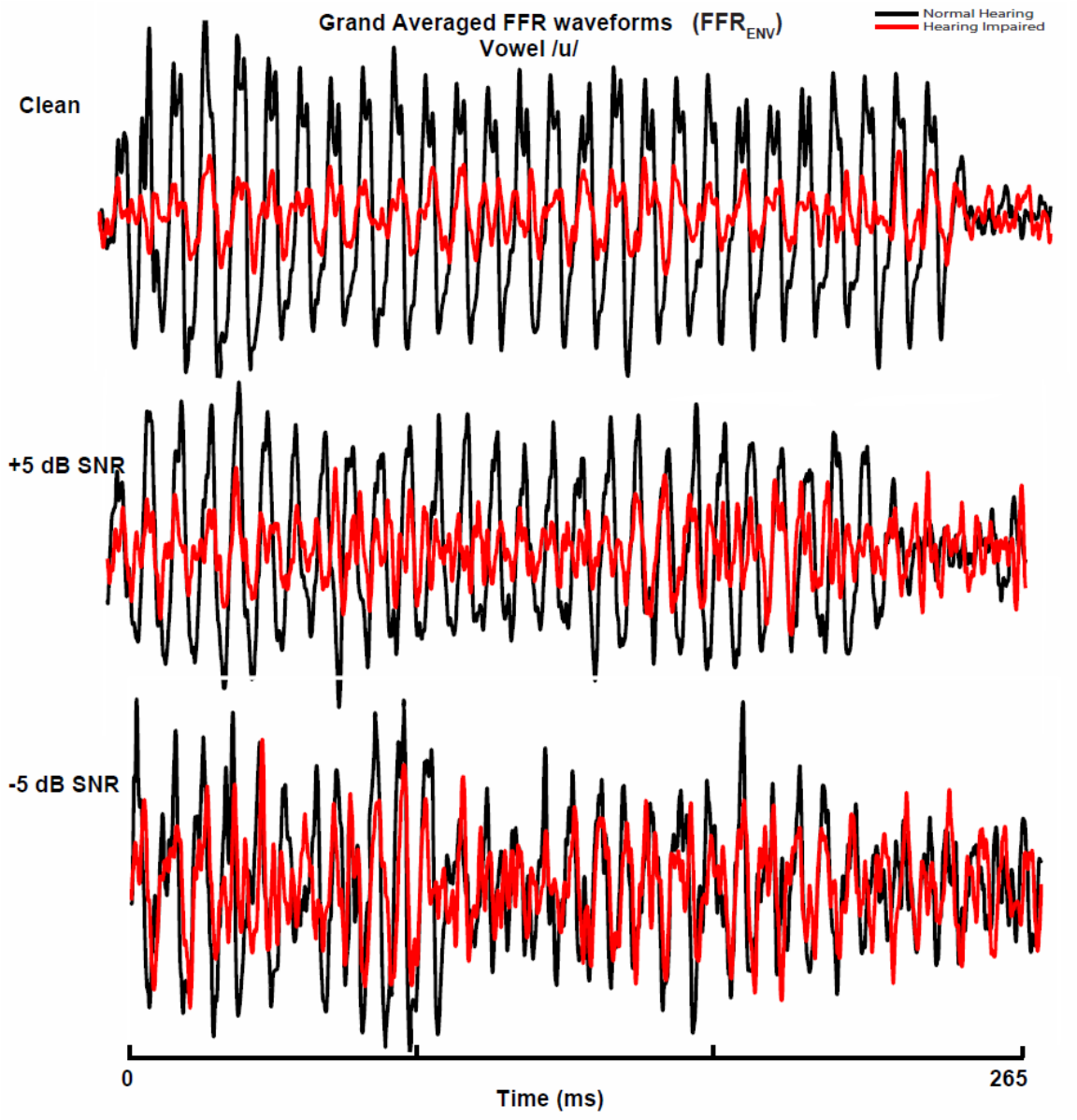

Figure 7.1: Grand averaged FFR waveforms for the envelope FFR for the vowel /u/ at different SNRs: clean (top), +5 dB SNR (center), -5 dB SNR (bottom). HI waveforms (red) are superimposed on NH waveforms (black).

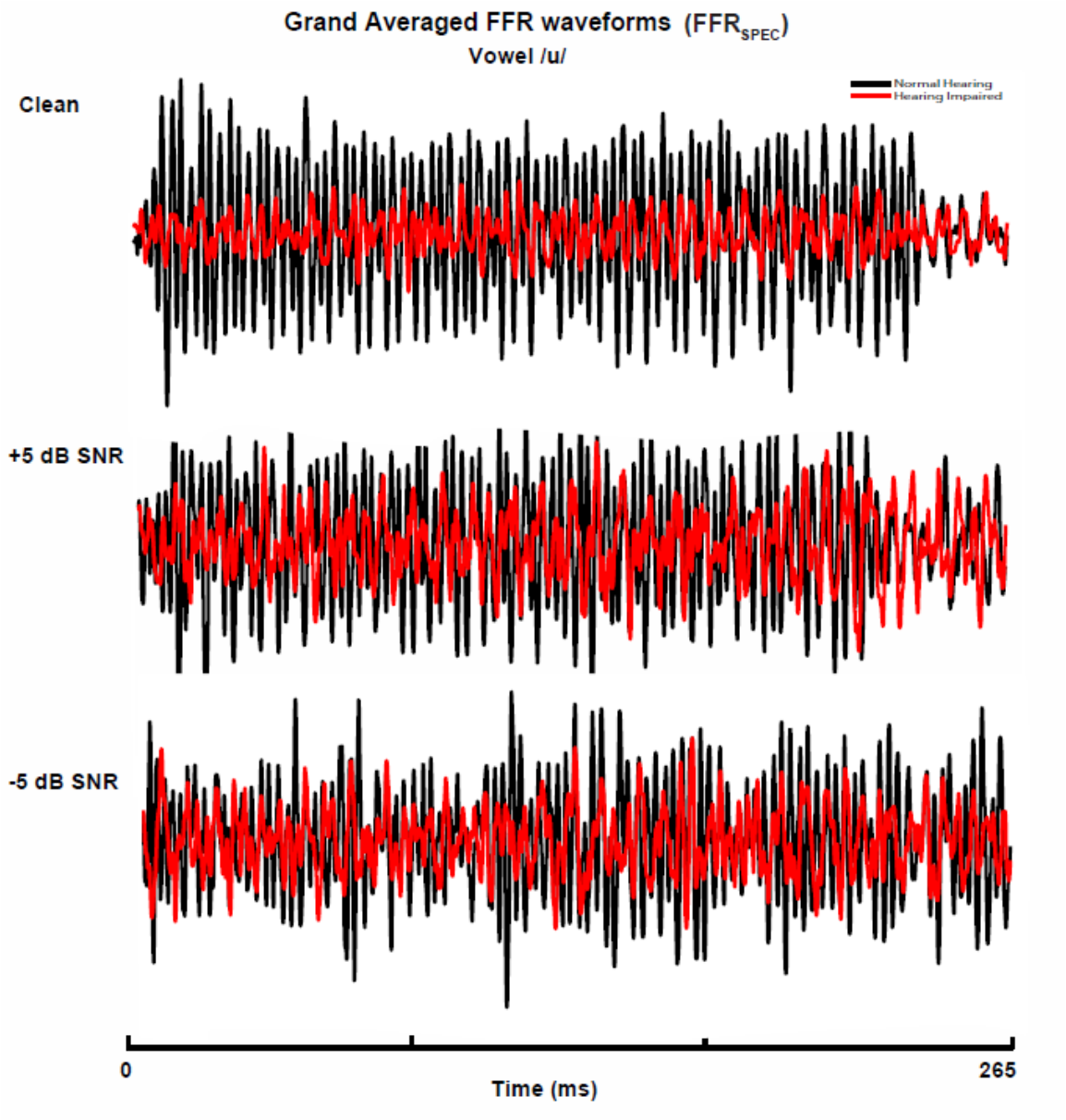

Figure 7.2: Grand averaged FFR waveforms for the spectral FFR for the vowel /u/ at different SNRs: clean (top), +5 dB SNR (center), -5 dB SNR (bottom). HI waveforms (red) are superimposed on NH waveforms (black).

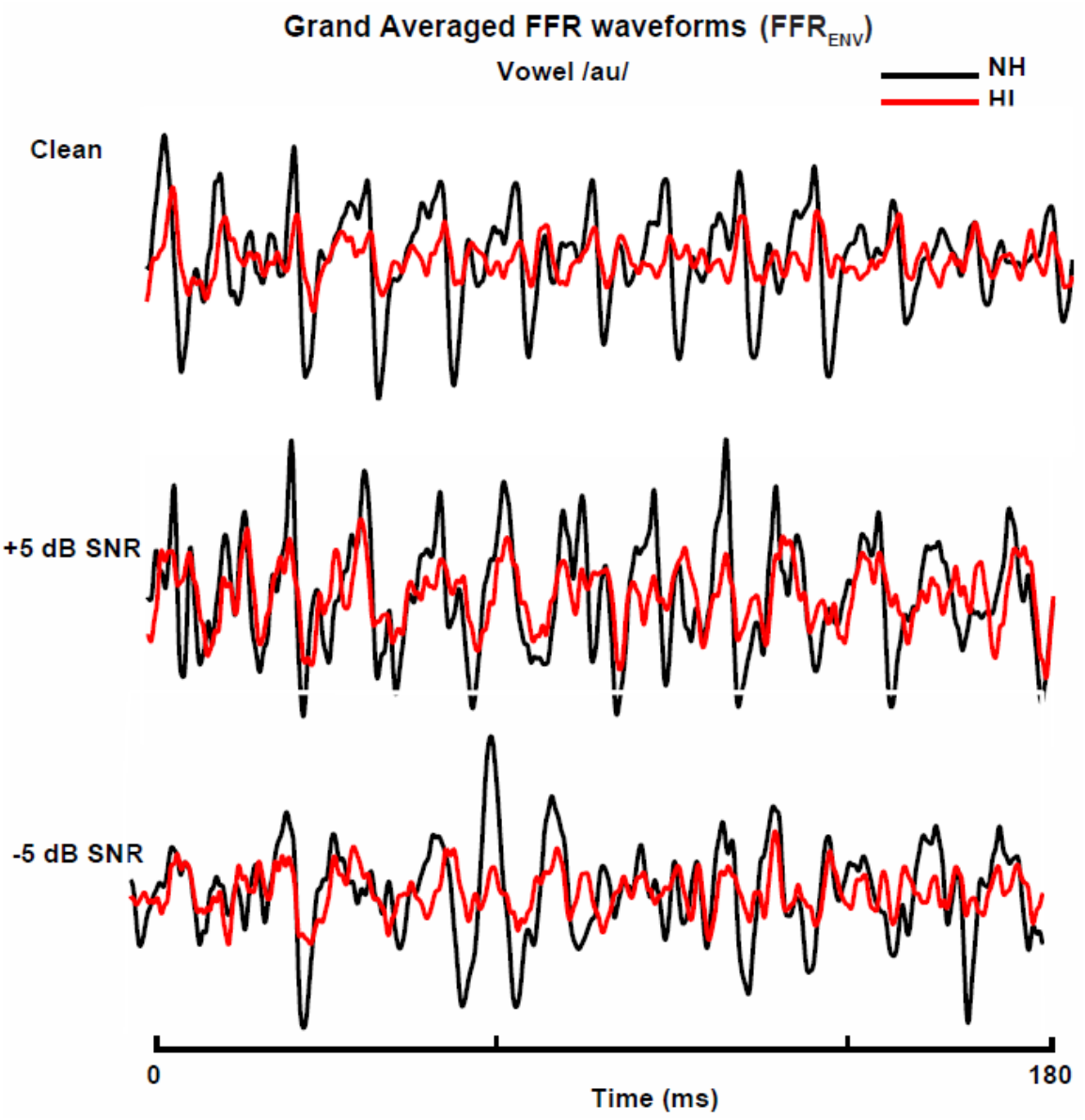

Figure 7.3: Grand averaged FFR waveforms for the envelope FFR for the diphthong /au/ at different SNRs: clean (top), +5 dB SNR (center), -5 dB SNR (bottom). HI waveforms (red) are superimposed on NH waveforms (black).

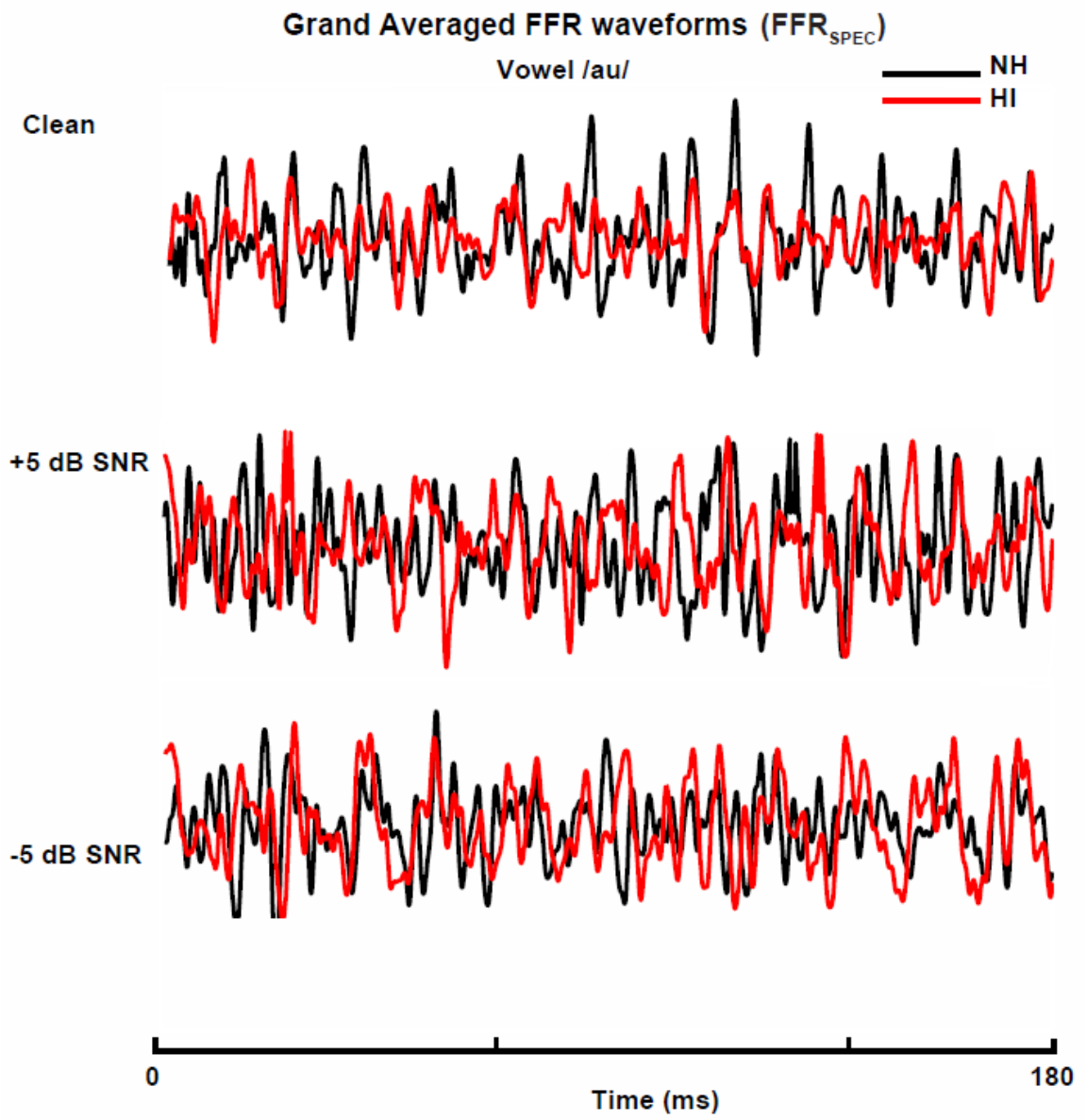

Figure 7.4: Grand averaged FFR waveforms for the spectral FFR for the diphthong /au/ at different SNRs: clean (top), +5 dB SNR (center), -5 dB SNR (bottom). HI waveforms (red) are superimposed on NH waveforms (black).

7.4.2 Grand averaged spectrograms and correlograms

A qualitative representation of the group and SNR differences in FFR_{ENV} is provided in the grand averaged spectrogram and correlogram analyses. Grand averaged autocorrelograms of the FFR_{ENV} waveforms were derived for the NH and the HI at each

SNR level are shown in Figure 7.5 (vowel /u/) and Figure 7.8 (diphthong /au/). Reflecting the pitch strength analysis qualitatively, stronger and clearer bands of phase locked activity are seen at the reciprocal of F0 in correlograms of the NH listeners than the HI listeners at all SNR levels. It can also be seen that the correlogram bands become weaker as SNR decreases from +5 to -5 dB.

Grand averaged spectrograms are summarized in Figures 7.6 and 7.7 for the vowel /u/ and Figures 7.9 and 7.10 for the diphthong /au/. While a band is seen at the F0 and F1 in the grand averaged FFR_{ENV} spectrograms of both the steady-state and the time-varying signal in both groups, the NH group shows robust activity at these stimulus relevant frequencies whereas there appears to be considerable spectral smearing in the HI group. The amount of smearing also increases within the NH and HI groups as SNR decreases.

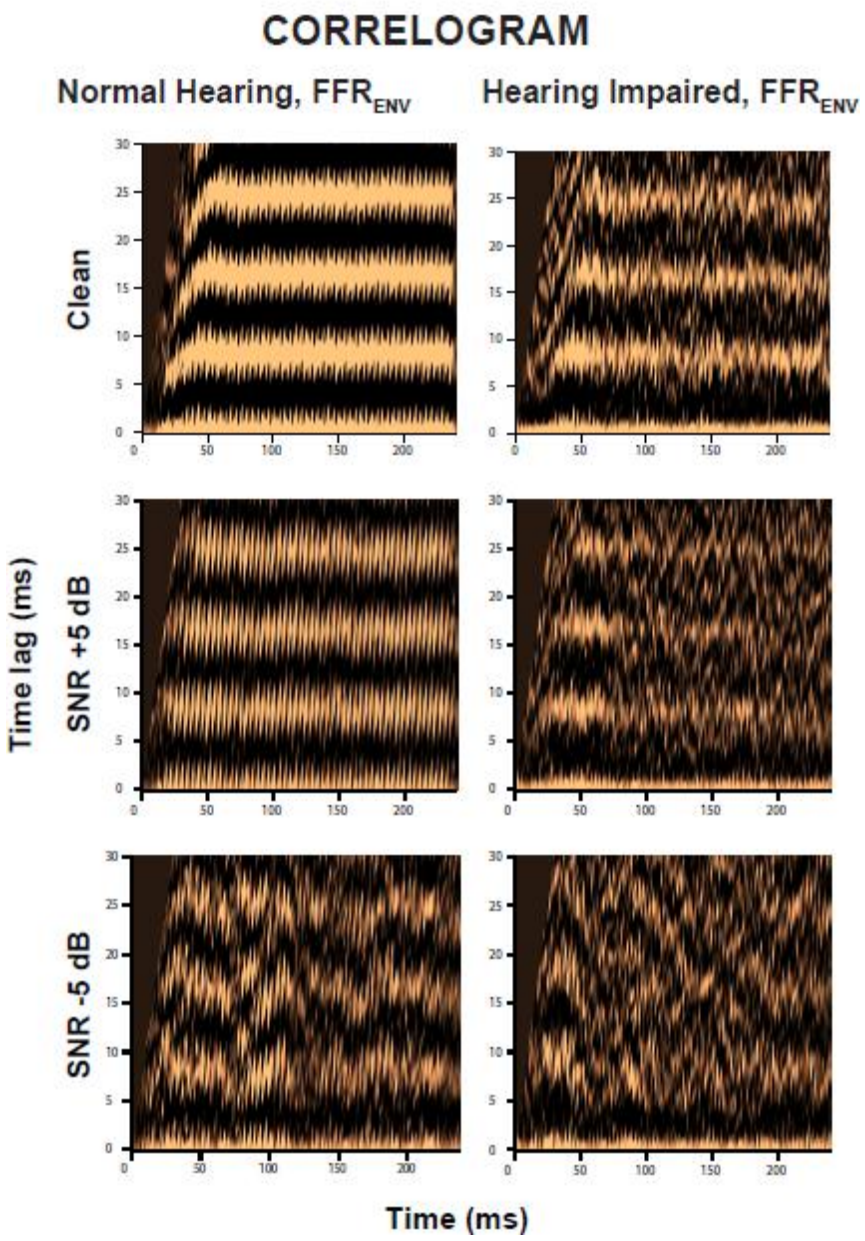

Figure 7.5: Correlograms for envelope FFR for NH (left) and HI (right) at clean (top), +5 dB SNR (middle) and -5 dB SNR (bottom) for the vowel /u/ (F0=120 Hz).

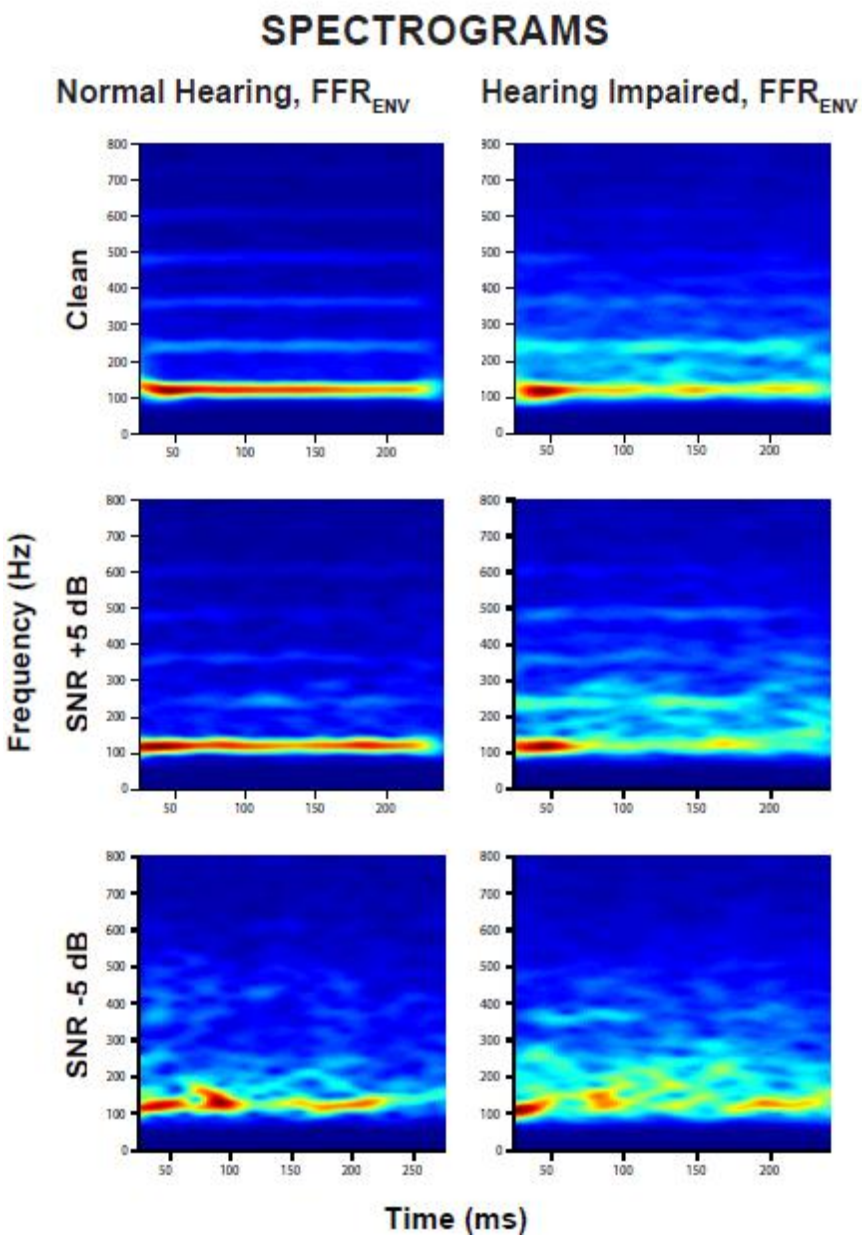

Figure 7.6: Spectrograms for envelope FFR for NH (left) and HI (right) at clean (top), +5 dB SNR (middle) and -5 dB SNR (bottom) for the vowel /u/ (F0=120 Hz).

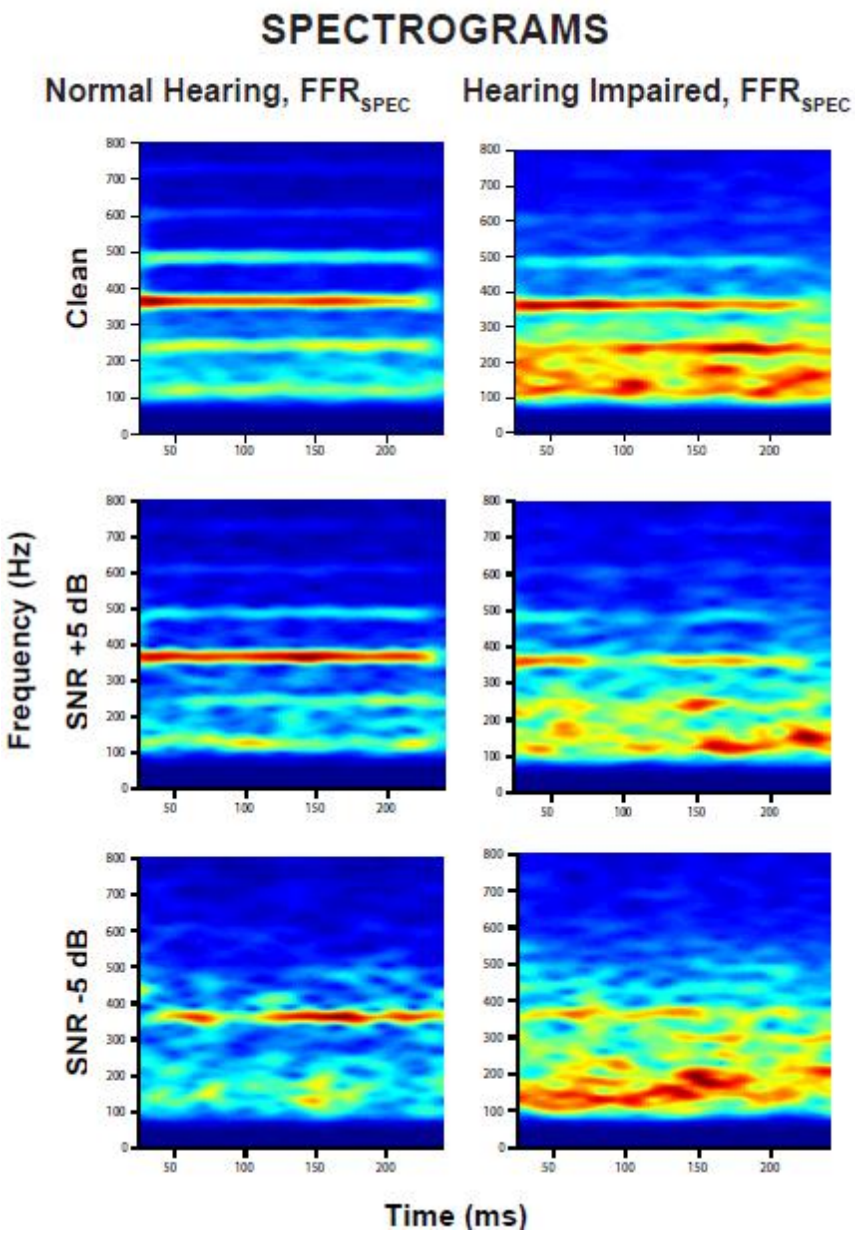

Figure 7.7: Spectrograms for spectral FFR for NH (left) and HI (right) at clean (top), +5 dB SNR (middle) and -5 dB SNR (bottom) for the vowel /u/ (F1=360 Hz).

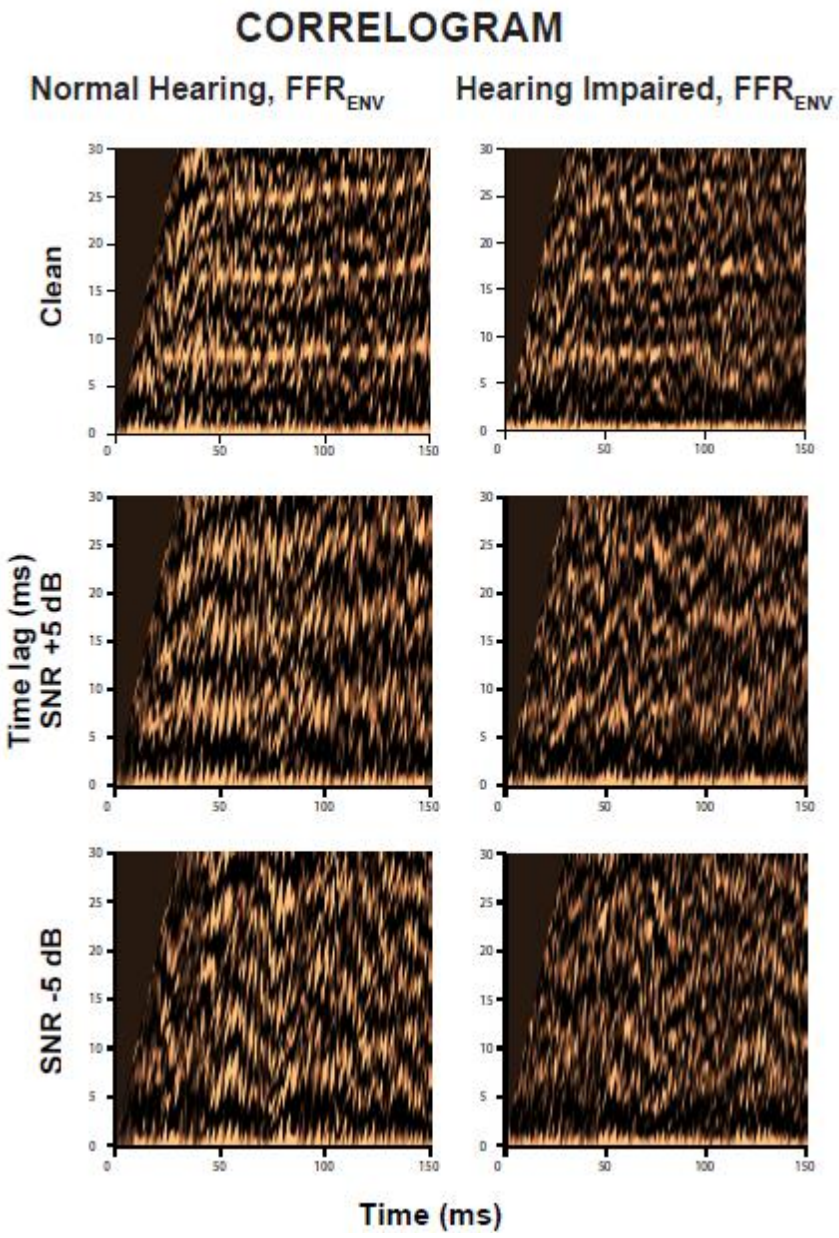

Figure 7.8: Correlograms for envelope FFR for NH (left) and HI (right) at clean (top), +5 dB SNR (middle) and -5 dB SNR (bottom) for the diphthong /au/.

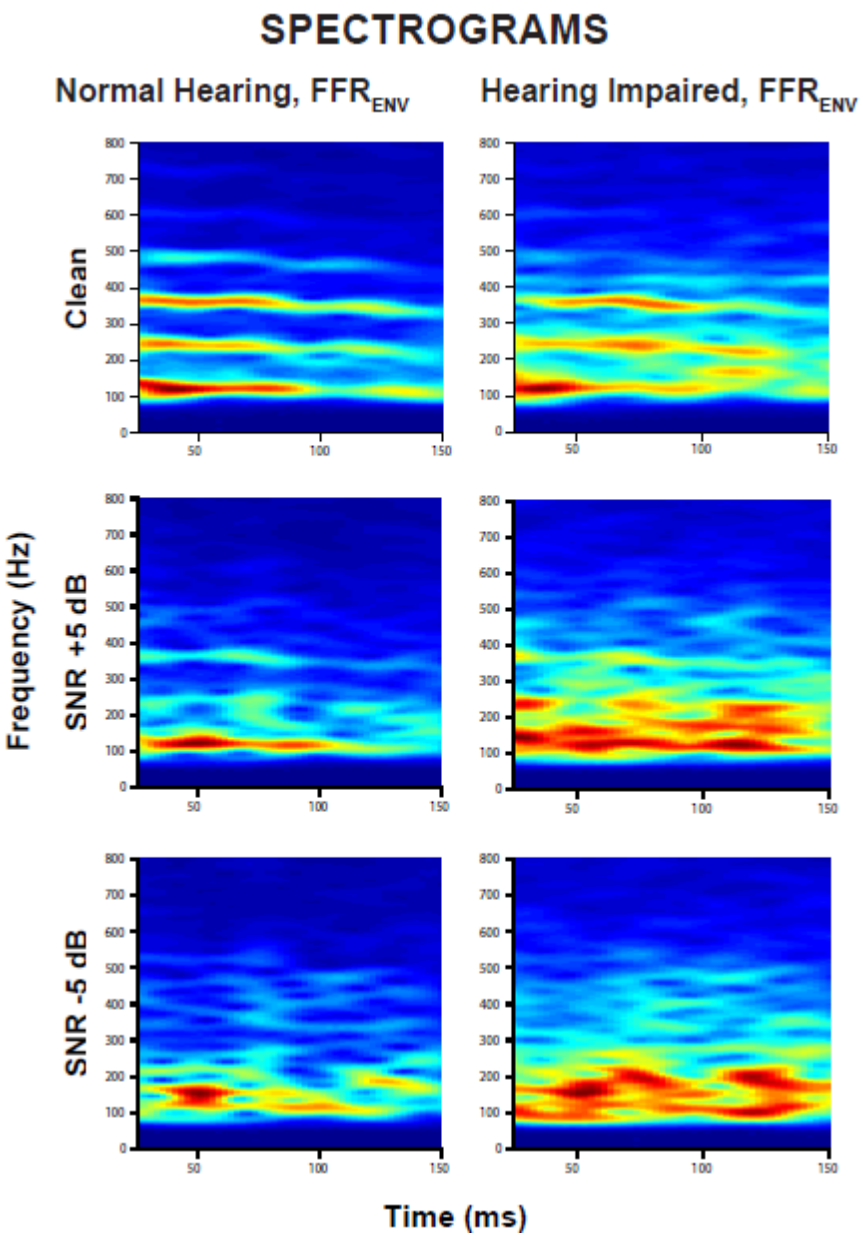

Figure 7.9: Spectrograms for envelope FFR for NH (left) and HI (right) at clean (top), +5 dB SNR (middle) and -5 dB SNR (bottom) for the diphthong /au/ (F0=114-120Hz).

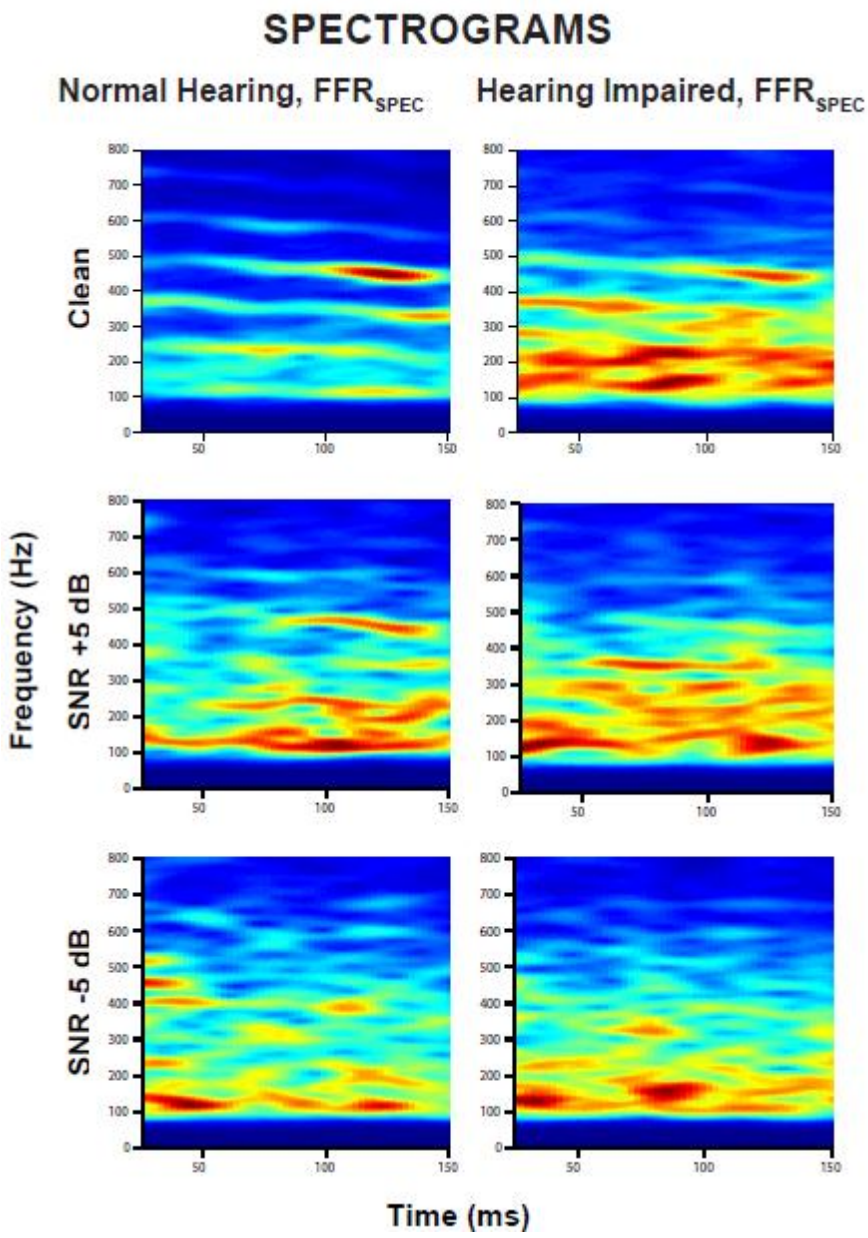

Figure 7.10: Spectrograms for spectral FFR for NH (left) and HI (right) at clean (top), +5 dB SNR (middle) and -5 dB SNR (bottom) for the diphthong /au/ (F0=114-120Hz).

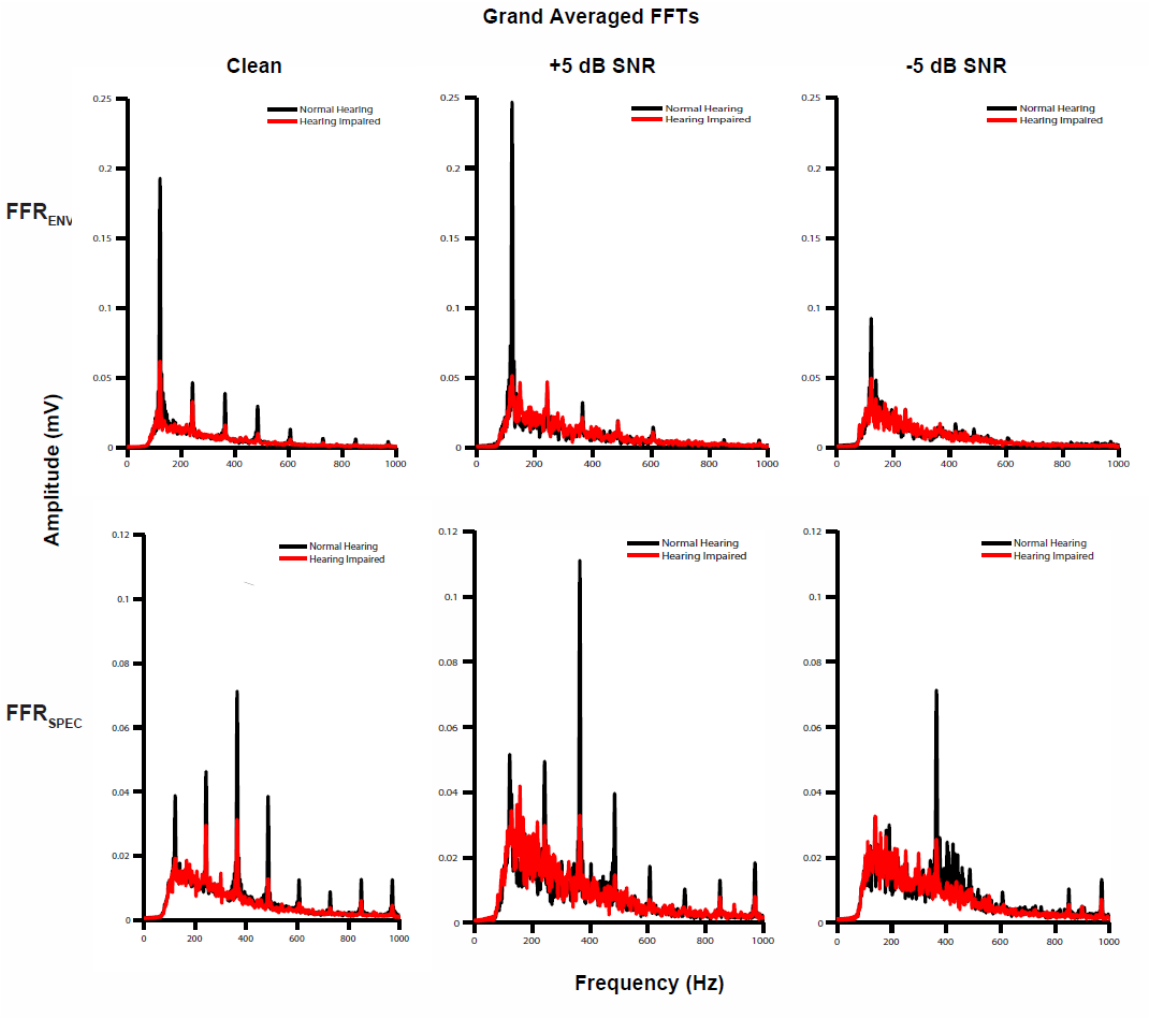

Figure 7.11: FFTs for envelope (top) and spectral (bottom) FFR for NH (black) and HI (red) at clean (left), +5 dB SNR (middle) and -5 dB SNR (right) for the vowel /u/ (F0=120 Hz, F1=360 Hz).

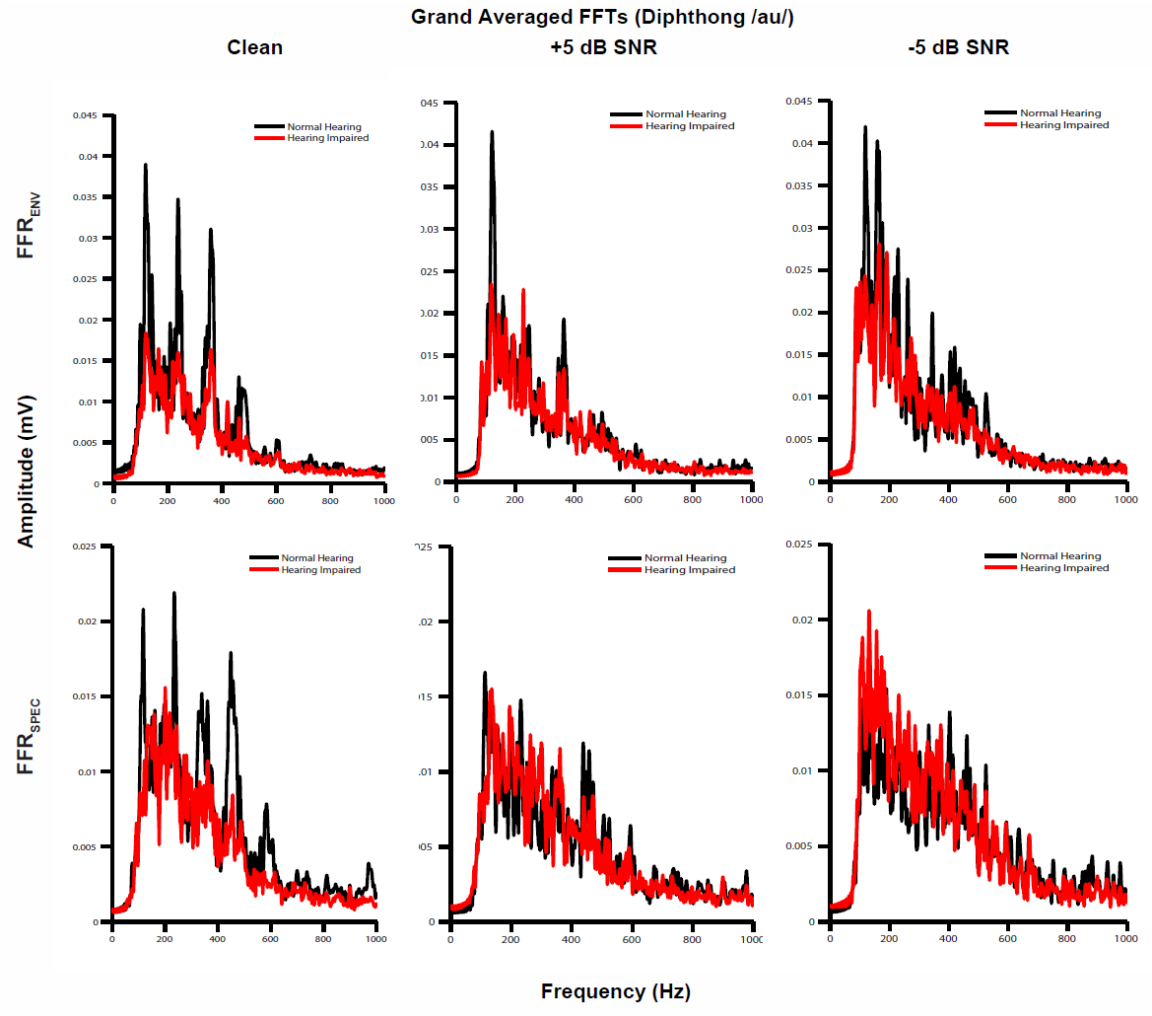

Figure 7.12: FFTs for envelope (top) and spectral (bottom) FFR for NH (black) and HI (red) at clean (left), +5 dB SNR (middle) and -5 dB SNR (right) for the diphthong /au/ (F0=114-120 Hz).

7.4.3 Effects of hearing impairment and SNR on subcortical neural encoding of envelope & TFS cues

A three way analysis of variance model with hearing loss, stimulus and SNR as the three factors was used to address the following questions: 1) is there a group difference between NH and HI listeners with respect to envelope encoding? 2) Is there an effect of stimulus (steady-state vs. time-varying) for NH and HI participant? 3) Is there

an effect of SNR for NH and HI participants? 4) Are there interaction effects between hearing loss, stimulus and SNR? The dependent variables for envelope and TFS encoding were stimulus-response spectral correlations in the FFR_{ENV} and FFR_{SPEC} conditions respectively. Stimulus-response spectral correlations were used as an index of FFR encoding of entire frequency range of the response, as opposed to measurements of FFR encoding strength at fixed frequency markers such as F0 and F1.

7.4.3.1 Effect of hearing loss and SNR on subcortical envelope encoding

For the FFR ENV condition, all main effects were statistically significant [hearing loss ($F(1,122)=47.98$, $P<0.0001$); stimulus $F(1,122)=24.47$, $P<0.0001$); SNR $F(2,122)=48.61$, $P<0.0001$). The three way interaction term between hearing loss, stimulus and SNR was not significant $F(2,122)=0.27$, $P=0.76$) nor was the SNR-stimulus interaction ($F(2,122)=1.75$, $P=0.18$). The interaction between hearing loss and SNR was significant ($F(2,122)=4.57$, $P=0.01$) while the hearing loss-stimulus interaction was marginally significant ($F(1,122)=2.54$, $P=0.0834$).

7.4.3.2 Effect of hearing loss and SNR on subcortical TFS encoding

Main effects of hearing loss ($F(1,125)=43.32$, $P<0.0001$) , stimulus ($F(1,125)=136.15$, $P<0.0001$) and SNR ($F(2,125)=10.53$, $P<0.0001$) were observed for the stimulus-response correlations in the FFR_{SPEC} condition. The three way interaction effect between hearing loss, stimulus and SNR was not significant ($F(2,125)=1.72$, $P=0.18$) nor were the interactions between hearing loss and SNR ($F(2,125)=1.21$, $P=0.30$)

or stimulus and SNR (F(2,125)=1.57, P=0.21). The interaction between hearing loss and stimulus was marginally significant (F(1,125)=3.40, P=0.06).

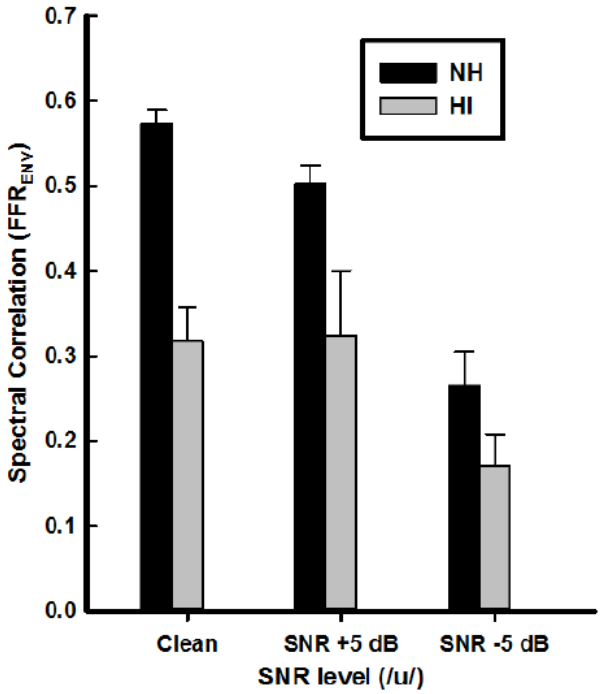

Figure 7.13: Stimulus-to-response spectral correlation for envelope FFR for NH (black) and HI (grey) as a function of signal to noise level for the vowel /u/.

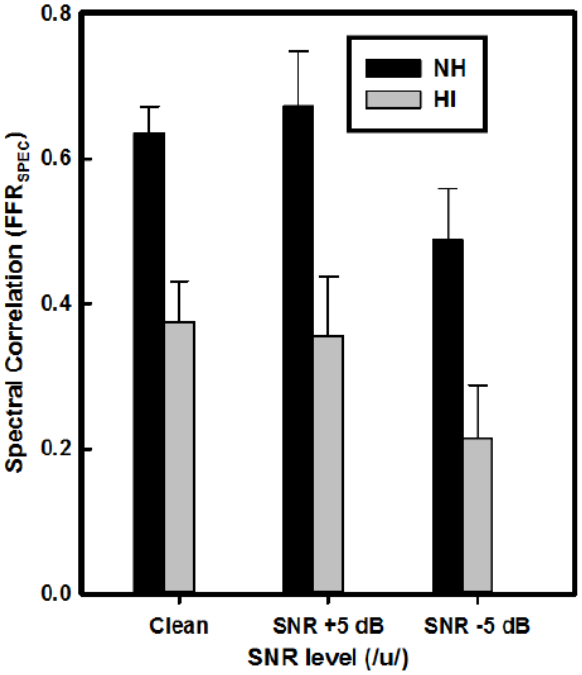

Figure 7.14: Stimulus-to-response spectral correlation for spectral FFR for NH (black) and HI (grey) as a function of signal to noise level for the vowel /u/.

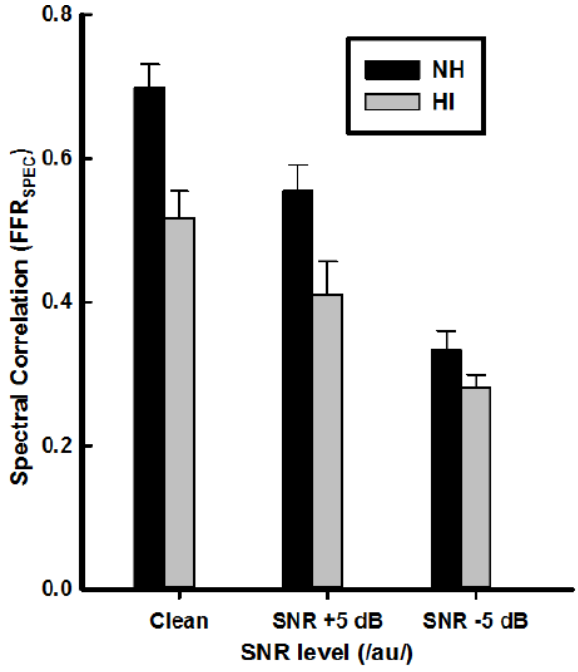

Figure 7.15: Stimulus-to-response spectral correlation for envelope FFR for NH (black) and HI (grey) as a function of signal to noise level for the diphthong /au/.

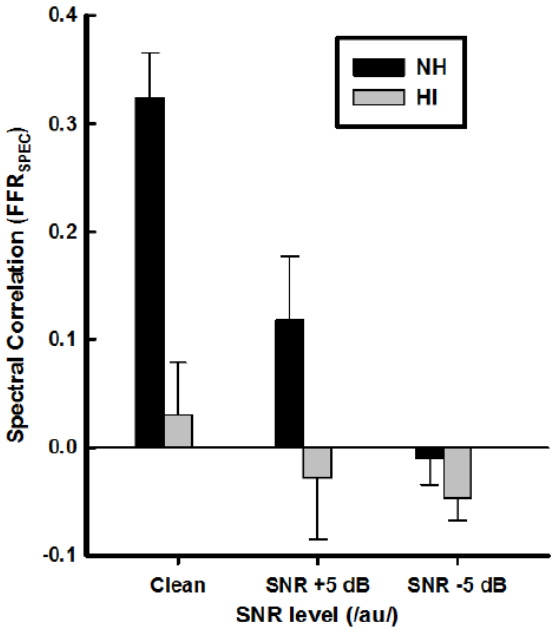

Figure 7.16: Stimulus-to-response spectral correlation for spectral FFR for NH (black) and HI (grey) as a function of signal to noise level for the diphthong /au/.

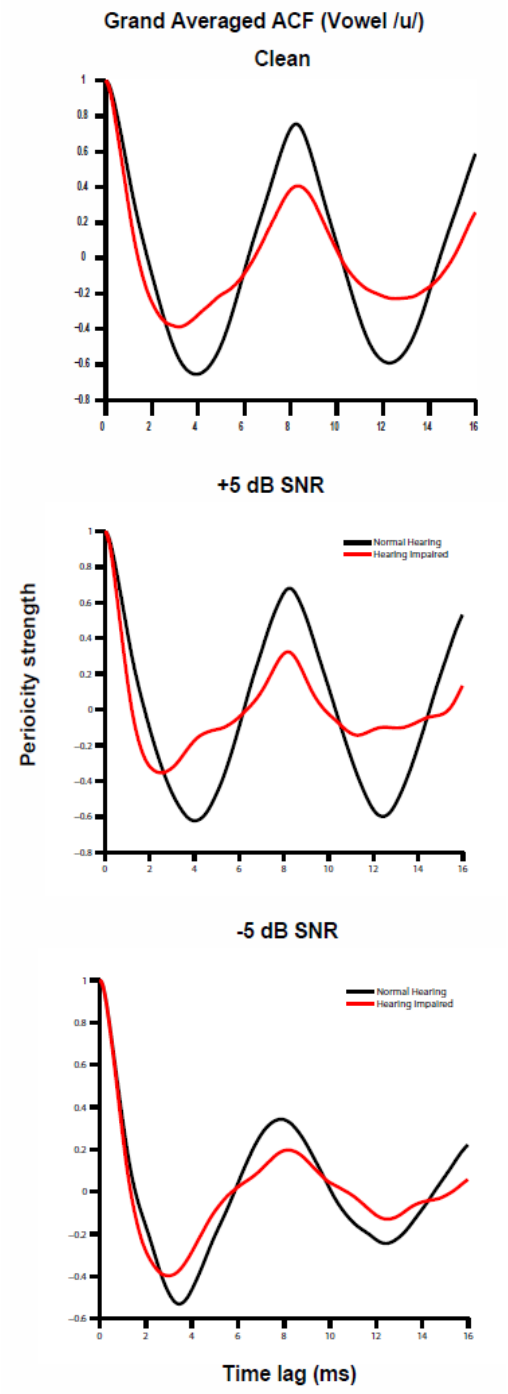

Figure 7.17: Grand averaged autorcorrelation functions for envelope FFR for NH (black) and HI (red) at different SNRs (Clean: top; +5 dB SNR: center; -5 dB SNR: bottom) for the vowel /u/.

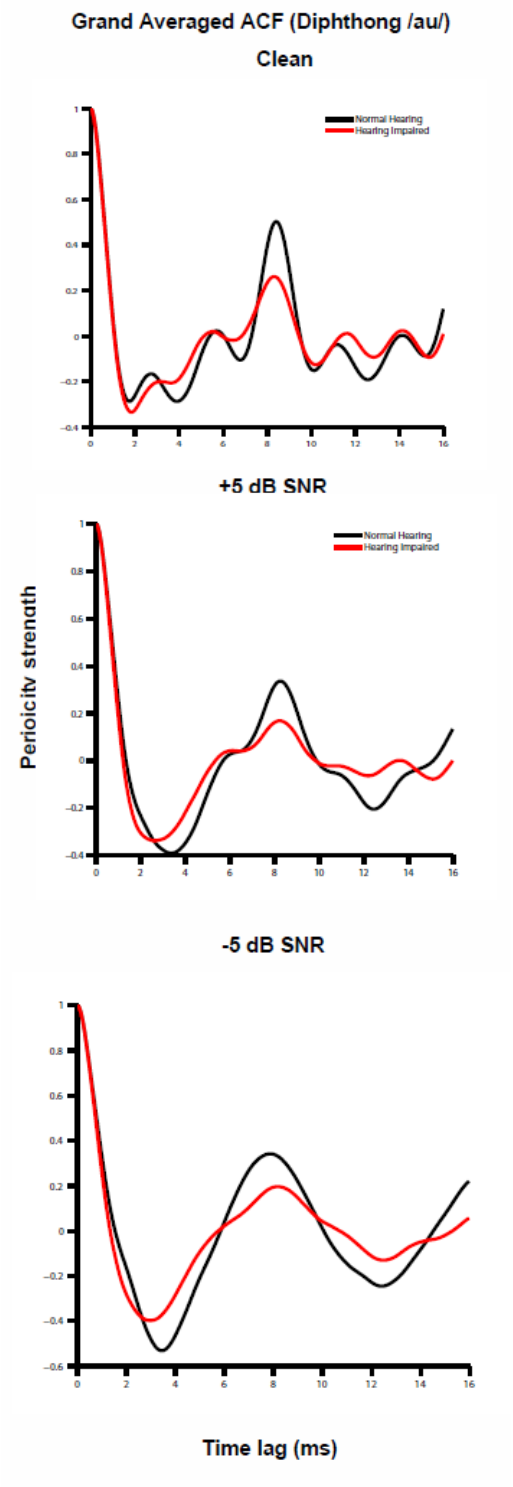

Figure 7.18: Grand averaged autorcorrelation functions for envelope FFR for NH (black) and HI (red) at different SNRs (Clean: top; +5 dB SNR: center; -5 dB SNR: bottom) for the vowel /u/.

7.4.4 HINT scores

A two-way ANOVA was used to analyze the HINT data (Figure 7.19). SNR (clean, +10, +5, 0, -5 dB) and hearing status (NH vs. HI) were the two independent variables and HINT scores acted as the dependent variable. Main effects were noted for both SNR ($F(4,89)=11.53$, $p<0.001$)and hearing status ($F(1,89)=12.30$, $p=0.0007$). Additionally, an interaction effect was noted between SNR and hearing loss ($F(4,89)=4.99$, $p<0.0011$). Further analysis of the interaction effect indicates that there are no differences as a function of SNR level in the NH speech perception performance. However, there is a definite decrease in the HINT score as SNR changes from the clean to the -5 dB condition. No differences are seen between NH and HI at any of the SNR conditions save the least favorable (-5 dB SNR).

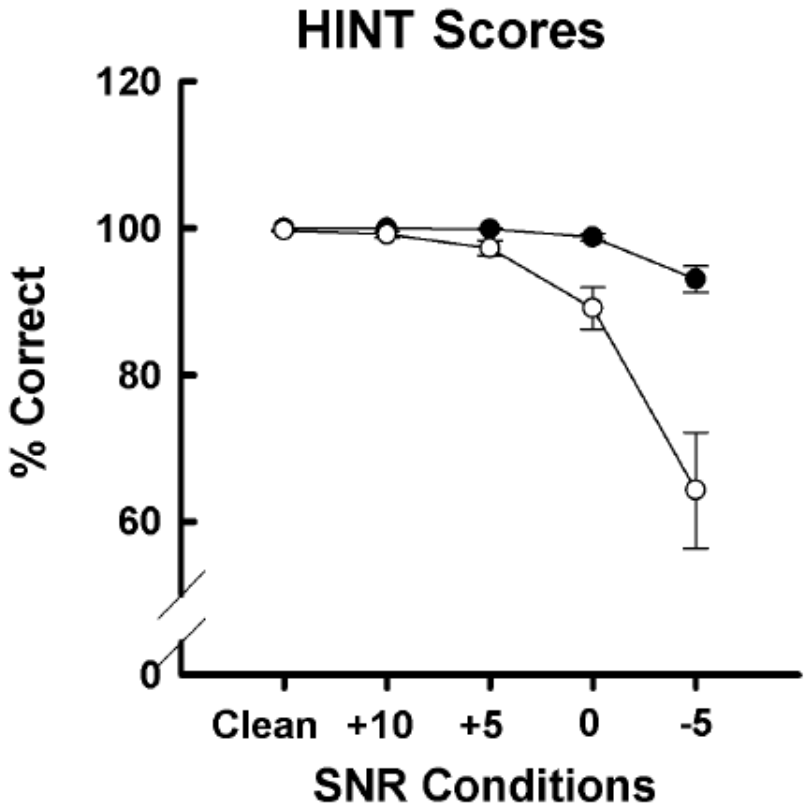

Figure 7.19: HINT scores in NH (filled circles) and HI (empty circles) at different SNRs

7.4.5 Summary

Effects of varying the SNR were readily seen in the NH group for both envelope and TFS encoding, in both time-varying and steady-state stimuli. Specifically, neural encoding in the clean and +5 SNR condition was consistently greater than neural encoding in the -5 SNR condition. While this effect was evident for across NH for envelope and formant-related FFR encoding, HI listeners exhibit minimal reductions in neural phase-locking as a function of SNR, as indexed by spectral correlation measures. However, SNR effects in the HI group are evident in the spectro-temporal data

visualizations (spectrograms and correlograms). A qualitative appraisal of the spectrograms in both NH and HI listeners shows a clear degradation of energy bands associated with the F0 and formant frequency as SNR decreases. Spectrogram and correlogram bands in both groups show a relative loss of energy in the bands of interest at F0 and formant frequencies as background noise increases. In addition, the HI spectrogram shows considerable spectral smearing and energy at spurious peaks as SNR decreases.

In addition to SNR effects, it is important to address effects of hearing loss. Differences between NH and HI subjects were always present for the clean conditions in both steady-state and time-varying stimuli for both envelope and TFS encoding. These findings are consistent with results from Experiment 1-3. However, effects of hearing loss seem significantly reduced, or in other words, there appears to be no statistically significant difference for spectral correlation when background noise is introduced. However, the differences between NH and HI subjects are clearly recognized in the spectrograms and correlograms for both stimuli (vowel & diphthong) at +5 and -5 dB SNRs. For the clean and +5 SNR levels, bands at stimulus-relevant frequencies are reduced in energy and spectrally smeared in the HI group as compared to the NH group. These differences are also seen in the -5 SNR condition to a certain extent; however SNR related effects tend to minimize the differences due to hearing loss at this level, and NH and HI spectrograms start resembling each other more.

7.5 Discussion

FFRs were collected in response to the steady-state vowel /u/ and a time-varying diphthong /au/ at three different SNR conditions: quiet (no noise), +5 SNR and -5 SNR. Overall, results indicate that FFR encoding of envelope and TFS is affected by effects of SNR, as well as hearing loss.

Reduced FFR strength with addition of background noise indicates a reduction in neural phase-locking ability in challenging listening conditions. Reduced neural-phase-locking ability in NH participants may be related to a loss of spectral contrasts related to decreasing SNR. For the HI subjects, reduced neural phase-locking may reflect the effects of loss of frequency selectivity and impaired neural synchrony related to hearing loss, and may be exacerbated by the added loss of spectral contrasts in background noise.

7.5.1 Effect of SNR on NH subcortical envelope & TFS encoding

For the NH group, a significant effect of SNR was observed for brainstem neural envelope encoding, consistent with other FFR studies examining SNR in NH. F0 magnitude decreased significantly as the SNR levels changed from clean to -5 dB SNR. Similar results were observed for TFS encoding (F1 magnitudes). These findings are consistent with results from Cunningham et al. (2001), Parbery-Clark et al. (2009) and Li and Jeng (2011), all of whom found degraded neural representations of F0 and F1 with increasing SNR. Further, no differences in envelope or TFS encoding were observed between the quiet and +5 SNR conditions, but a sharp drop occurred at -5 dB SNR. These findings indicate that neural phase-locking is relatively unaffected as long as the target signal is at or above the competing signal, consistent with Li & Jeng (2011), Song et al.

(2010) and Russo (2004) who found that the FFR is well preserved at 0, 5 and 10 dB SNR. These results are also consistent with perceptual studies which show that speech understanding in background noise is largely unaffected for SNRs of 0 dB or greater, as is formant tracking in multitalker babble in NH listeners. The degradation in FFR in the -5 SNR condition may be related to upward spread of excitation with the addition of noise and a loss of spectral contrast.

7.5.2 Effects of SNR on HI subcortical envelope & TFS encoding

Neural encoding of both envelope and TFS encoding was degraded in the HI subjects as compared to NH subjects.

Reduced TFS encoding with background noise is consistent with established neurophysiologic and behavioral literature. Henry & Heinz (2013) demonstrated that reduced TFS encoding in the presence of background noise in chinchillas with NIHL may be associated with a downward shift in frequency tuning of TFS and envelope encoding in CFs of neurons. As a result of this downward shift, all nerve fibers, irrespective of CF, begin to encode low frequency TFS information (which includes background noise) while high frequency TFS (>2.5 kHz) was not encoded. Other animal neurophysiologic studies have demonstrated similar frequency encoding shifts in the inferior colliculus (Willott, 1981). It is possible that reduced TFS encoding as indexed by the FFR in the HI subjects in the present experiment could reflect impairments in neural synchrony following hearing loss induced tonotopic remapping.

The loss of formant capture in HI cats has been attributed to disruptions in neural synchrony (Miller et al., 1997). Formant capture has been reported in subcortical neural

encoding of TFS in NH subjects (Krishnan, 2002; Chapter 4). In Chapters 4 and 5, a loss of formant capture was noted in the HI FFR. Hence, reductions in TFS encoding in background noise in HI subjects may reflect, to a certain extent, a loss in formant capture subsequent to disrupted neural synchrony.

Reduced TFS encoding is also consistent with various vowel and diphthong perception studies. Adding background noise is known to cause upward spread of excitation as well as a decrease in spectral contrast in resulting auditory excitation patterns in NH listeners. Wider auditory filter bandwidths in hearing impairment may distort representation of formant frequencies by reducing spectral contrasts further and indirectly reducing the internal SNR.

In the present study, envelope encoding in hearing impairment is reduced as compared to NH listeners, inconsistent with single unit data from Henry & Heinz (2013). Findings from Henry & Heinz suggest that while there is a downward shift in frequency tuning of TFS encoding in the HI animals, envelope encoding remains tonotopically organized and is unaffected. It is possible that some portion of the reduced envelope encoding seen in the present study is a consequence of reduced audibility, as the stimuli were presented at equal SPL and not equated for audibility. This may be further explained by the impact of high frequency hearing loss on the role of unresolved harmonics in detecting envelope information. It has been established by neurophysiologic studies at the single unit level as well as at the subcortical level with the FFR that F0 discrimination is mediated by interactions between unresolved harmonics in the high frequency regions of the basilar membrane. Further, temporal envelope cues play a dominant role in speech perception and encoding in HI listeners as they have reduced

access to resolved harmonics. However, F0 discrimination abilities are best correlated with audiometric thresholds at higher frequencies, where these listeners typically have greater hearing loss (Summers & Leek, 1998). Therefore, it is possible that the reduced neural F0 encoding seen in the present study is due to increased audiometric thresholds (low audibility) at higher frequencies.

However, reduced envelope encoding by HI in background noise may not be reflective of just audibility. F0-based source segregation abilities are sometimes affected even in NH listeners, evident in their inability to separate multiple pitches when presented with concurrent stimuli containing only unresolved harmonics (Carlyon, 1996; Micheyl, Bernstein & Oxenham, 2006). It is reasonable to hypothesize that HI individuals relying predominantly on temporal envelope cues arising from interaction of unresolved harmonics may experience similar, if not worse, inabilities in source segregation. Hence, reduced F0 encoding in the presence of background noise may be a result of poor source segregation in hearing loss.

7.5.3 Effect of age on subcortical encoding of envelope and TFS cues:

As subjects in the present study were not age-matched, it is possible that some of the effects observed in the present study may be related to age-related differences. The effects of aging do not affect encoding of low frequency stimuli in the FFR (Clinard et al., 2010); however, the stimuli in this study were presented in quiet, whereas background noise of varying levels was used in the present experiment. There is no literature examining the effect of aging on the subcortical FFR collected in background noise. However, the overwhelming conclusion from perceptual and neurophysiologic studies

suggests that aging affects speech understanding and encoding when stimuli are presented in challenging backgrounds (Gordon-Salant, Yeni-Komshian, Fitzgibbons, & Barrett, 2006; Pichora-Fuller & Singh, 2006). Hence, the role of age in FFR encoding of speech sounds in background noise in NH and HI individuals cannot be ruled out for the results of the present experiment.

Summarily, differences seen across SNR conditions in envelope and TFS encoding in HI subjects may be due to a combined effect of reduced SNR and degraded phase-locking consequent to reduced audibility, decreased frequency selectivity, impaired phase-locking synchrony and aging effects.

7.5.4 Efficacy of analysis metrics

The mismatch between the analysis metric (stimulus-response correlation) and spectro-temporal data visualizations is puzzling. It is to be noted that this metric shows appropriate results that correspond to the spectrogram and correlogram visualizations when measuring SNR effects in NH individuals, as well as differences between NH and HI individuals in quiet. Bearing these observations in mind, it appears that stimulus-response correlation is not well suited as an analysis metric to examine effects of neural phase-locking *in HI subjects in the presence of background noise*. The stimulus-response correlation measurements were chosen over original measures of F0 and harmonic related magnitude as they provide an overall spectral picture of FFR encoding as opposed to magnitudes at isolated harmonics. These correlation measures have been used to index FFR encoding and correlate well with pitch strength, F0 magnitude and harmonic magnitude measurements in Chapter 4. Further, the spectral correlation measurements

were designated as the method of choice *after* using the original FFT peak picking techniques used in Experiments 1-4. FFT peak measurements proved to be unreliable for the HI subjects. The addition of noise created challenges with respect to picking peaks at the F0 and harmonics; peaks were reduced in magnitude, with a much broader lobe, as compared to the sharp FFT peaks typically seen in NH and occasionally absent or misplaced in the response spectrum. Overall, these observations suggest that traditionally used FFR analysis techniques are not well-equipped to measure neural phase-locking accurately in HI listeners in degraded listening conditions.

The challenges experienced in identifying response components in background noise are not unique to the present experiment. Various studies investigating the effects of background noise on brainstem potentials indicate a decrease in response amplitude and morphology (Yamada et al., 1979; Burkard and Hecox, 1983; Cunningham et al., 2001; Russo et al., 2004;Parbery-Clark et al., 2009; Song et al., 2010; Li and Jeng, 2011). Low response amplitudes render identification of response components significantly challenging, even after a large sweep count (Anderson et al., 2010). Hence, alternate methods of data analysis should be strongly considered for measuring subcortical speech encoding in hearing impairment. Tierney, Parberry-Clark, Skoe & Kraus (2011) describe the application of an objective automated method of determining frequency specific phase shifts in the neural response known as the "cross-phaseogram" to brainstem latency shifts. Specifically, this method entails comparing frequency specific phase shifts with latency shifts in manually selected response components. Based on the spectro-temporal data visualizations of the data from the current experiment which

appear to be sensitive to SNR effects, the power spectrum density may be another analysis metric potentially worth exploring.

7.5.5 Brain-behavior relationships

The effects of hearing loss and SNR level on the HINT scores are somewhat different from those observed on the FFR. The results of the HINT suggest that background noise affects sentence perception in HI but not in NH listeners, whereas background noise affects neural encoding in both NH & HI subjects. Also, effects of hearing impairment which are restricted to the least favorable SNR condition, suggest that HI listeners are not significantly affected by background noise until the level of the noise is equal to or greater than the target signal. However, group differences between NH and HI are observed at any given SNR for neural data. It is possible that the differences observed between the HINT and FFR are due to the differences in stimulus material (sentences in HINT vs. vowel in the FFR). Additionally, the FFR reflects pre-attentive sensory level processing, which may be more sensitive to the effects of noise and hearing loss. Speech perception tested using HINT sentences reflects not just auditory ability, but also higher level processes, which enable the listeners to use contextual cues, cognition and memory to "fill in the blanks" even when they are not quite sure of the target signal.

7.6 Conclusions

Most individuals with hearing loss experience difficulty understanding speech in challenging listening situations such as background noise. Findings from the present experiment contribute to our currently limited knowledge of the neural correlates of

perceptual deficits in adverse listening conditions. Understanding the neural underpinnings of hearing in noise may hold the key for design of improved signal processing strategies in amplification devices.

Overall, results from this study are consistent with established behavioral and neurophysiologic literature.

- Spectral correlation results showed an increase in degradation of brainstem neural representation of envelope and TFS as SNR decreased for both groups with more robust representation for the NH group at SNRs greater than 0.
- Subcortical neural encoding degrades as a function of SNR in NH listeners for both envelope and TFS, likely due to a loss in spectral contrasts and upward spread of masking.
- Traditionally used measures of autocorrelation and FFT analyses are not sensitive to SNR induced changes in subcortical neural encoding in HI subjects. Alternate measurement techniques must be explored and/or developed.
- Spectro-temporal data visualizations of HI FFRs across SNR conditions underline the combined effect of increasing background noise superimposed on an impaired system.
- Subcortical neural encoding of envelope and TFS in HI in background noise is likely a combination of lack of audibility, poor frequency resolution, loss of spectral contrasts, impaired neural synchrony, high frequency hearing loss and aging effects.
- A dissociation is noted between subcortical neural encoding and behavioral perception of speech in noise. Such a dissociation may be reflective of the greater

sensitivity of the FFR as a pre-attentive sensory response compared to higher level processing reflected in the speech perception task. Differences in stimuli may also contribute towards the observed dissociation.

CHAPTER 8. EFFECTS OF REVERBERATION ON SUBCORTICAL NEURAL ENCODING OF ENVELOPE & TFS CUES IN HEARING IMPAIRMENT

8.1 Introduction

8.1.1 Motivation

Reverberation is a commonly encountered adverse listening condition that causes significant speech perception deficits in HI listeners. Reverberant speech is a combination of the original signal and time-delayed, scaled reflections of the signal, leading to a temporally smeared representation at the listener's ear (Assmann & Summerfield, 2004).

Reverberation effects can be classified into two main categories: overlap masking and self-masking (Bolt & MacDonald, 1949). Overlap masking is similar to the concept of forward masking, where energy from a previous sound segment masks a subsequent sound segment. Self-masking refers to masking effects caused by reverberation-related temporal smearing. Nabalek et al. (1989) offer a detailed review of both these concepts.

Assmann and Summerfield (2004) provide an excellent summary of the effects of reverberation. Transformation of dynamic features of the signal spectrogram into static features is the primary characteristic of reverberation. For e.g., monophthongization of diphthongs occurs due to flattening of formant transitions in time-varying diphthongs. Reverberation also causes prolongation of sounds (Nabalek et al., 1986); such prolongation can affect both duration and spectral characteristics of time-varying formant frequencies. An increase in duration, as seen in reverberation, causes frequency glide

spectra to become broader, and alters the pitch of the frequency glide. Specifically, the perceived pitch corresponds to the mean frequency for a short frequency transition but is shifted upward or lower in the direction of the frequency transition when duration is increased. In other words, if formant transition is in the upward direction, the perceived pitch is weighted towards higher formants; for a downward formant transition, the perceived pitch is weighted towards lower frequencies. Additionally, low frequency energy in the speech spectrum is enhanced by echoes created by reverberation, which can cause upward spread of masking. The effects of reverberation are distinct from masking in that reverberation affects spectro-temporal features of the stimulus whereas noise masking results from the addition of noise to the target signal (Bidelman & Krishnan, 2010; Nábělek & Dagenais, 1986)

Time-varying signals are affected to a much greater extent than steady-state signals by reverberation, as they are characterized by rapid frequency transitions that get smeared to a greater extent than time-invariant signals. Overlap of time-varying cues from earlier time points and later time points causes spectral smearing that reduces harmonicity cues.

Reverberation also has a significantly greater impact on speech perception in HI listeners as compared to NH listeners (Duquesnoy & Plomp, 1983; Finitzo-Hieber & Tillman, 1978).

The motivation for the present study lies in findings from perceptual and neurophysiologic experiments that have established effects of reverberation on speech perception and encoding in NH and HI. The following section discusses in detail results

from these perceptual experiments, single unit studies and FFR data, thereby laying the foundation for the design of the current experiment.

8.1.2 Behavioral studies examining the effect of reverberation on envelope & TFS cue perception in hearing loss

Nábělek and her colleagues have conducted a series of behavioral experiments (Nábělek & Dagenais, 1986; Nábělek et al., 1996; Nábělek & Robinson, 1982; Nábělek, 1988; Nábělek et al., 1989) examining effects of hearing loss and age on vowel and diphthong identification in quiet, noise and reverberation. Nábělek & Dagenais (1986) and Nábělek et al. (1989) documented reduced vowel and diphthong identification in reverberation as compared to quiet listening conditions in HI listeners. Error patterns for monopthongs and diphthongs were different in reverberation, with monopthongs being confused amongst themselves, while diphthongs were confused with their initial monopthongs. Errors in identification of monophthongs in HI were attributed towards prolonged stimulus duration and differential weighting of formant transitions in the reverberant conditions. Specifically, greater weighting was observed at higher frequencies for upward formant transitions and greater weighting for lower frequencies for downward formant transitions.

Diphthong confusions were not as frequent as monophthong confusions in reverberation. Predominant diphthong confusions observed were /au/-/ai/ and /ai/-/au/. Such confusions suggested that diphthongs, when confused, were most likely identified on the basis of the beginning monophthong. It is possible that the final segments of the

diphthong were masked by reverberation related temporal smearing, causing them to be identified as monophthongs.

Nábělek (1988) studied the effects of age and hearing loss on vowel identification in quiet and degraded conditions such as reverberation. Vowel identification was found to be significantly correlated with measures of hearing loss indexed by audiometric threshold averages, more strongly for the degraded conditions as compared to the quiet condition. While age was not correlated with vowel identification in quiet, both age and hearing loss were strongly correlated with vowel identification in reverberation.

As established by Nabalek et al. (1989), self-masking plays a major role in vowel confusions in reverberant conditions, where overlap masking due to preceding components is less likely. Consonant identification in reverberation is influenced by both overlap and self-masking. In addition, the authors found that reverberation caused masking of coarticulatory segments between /s/ and the following consonant in a /s_at/ stimulus construct.

Nábělek et al. (1994) studied the effects of relative intensity of transition segments on diphthong identification (/ai/) in NH and HI listeners in quiet and degraded conditions (noise and reverberation). Attenuation of the transition segment was varied from 0-15 dB. Findings indicated that diphthong identification was largely unaffected with varying attenuation of the transition segment in both groups in the quiet condition, but diphthong/monophthong confusions consistently occurred in both noise and reverberation where /ai/ was identified as /a/. Reverberation effects were stronger than noise effects for both groups. HI listeners tended to make diphthong/monophthong confusions with lesser amounts of attenuation on the transition segment than NH listeners.

Overall, these results indicate that changing the intensity of the transition segment significantly affects diphthong identification in reverberation. Nábělek et al. (1994) also established the importance of the F2 transition in diphthong identification. Specifically, for correct identification of the diphthong /au/, F2 transition segment was required to be at least 8 dB above the steady-state segment in the reverberant condition.

8.1.3 Neurophysiologic studies examining the effect of reverberation on envelope & TFS cue encoding in hearing loss

Sayles and Winter (2008) studied the effects of reverberation on time-varying pitch encoding of complex tones in single unit responses at the level of the ventral cochlear nucleus in guinea pigs. Results of the study indicated that F0 encoding by neurons tuned to low characteristic frequencies is resistant to the effects of reverberation. However, neurons tuned to higher characteristic frequencies demonstrated reduced F0 encoding as a function of reverberation. Similarly, a significant increase in the F0DL threshold with reverberation was observed in human subjects when provided with only envelope modulation cues from high frequency channels. According to Cariani and Delgutte (1996a, 1996b), Meddis and O'Mard (1997) and Sayles and Winter (2008), TFS information is extracted primarily from resolved harmonics while envelope information from the interaction of unresolved harmonics. Reverberation causes a randomization of phase relationships between unresolved harmonics (Sayles & Winter, 2008), which results in a greater degradation in pitch cues that are extracted from the unresolved regions.

8.1.4 Electrophysiological (FFR) studies examining the effect of reverberation on envelope & TFS cue perception in hearing loss

While several experiments explore the effects of subcortical pitch processing of degraded acoustic inputs such as signals in background noise, there is currently only one study in the literature (Bidelman, & Krishnan, 2010) that examines the effect of reverberation on the brainstem FFR. Bidelman & Krishnan (2010) investigated differences in FFR encoding between musicians and non-musicians for stimuli presented under varying conditions of reverberation. The stimulus was a synthetic vowel /i/ with time-varying F0 and steady-state formants presented in a "dry" (no reverberation) and mild, medium and severe reverberant conditions. Time domain convolution of the original signal with room impulse responses recorded in a corridor at varying distances was used to generate the three different reverberant conditions (mild, medium and severe), similar to the procedure described in Sayles and Winter (2008). Findings from Bidelman & Krishnan (2010) indicate that reverberation significantly affects subcortical encoding of formant related harmonics, while F0 encoding is fairly resistant under varying reverberant conditions. A significant effect of experience dependent neural plasticity was evident in the enhanced representation of F0 and F1 related harmonics in musicians as compared to non-musicians. Additionally, Bidelman & Krishnan (2010) found a strong correlation between neural encoding and behavioral F0 discrimination. Similar to the FFR data, F0 discrimination did not change significantly from the dry compared to reverberant listening conditions, while a definite increase in difference limen threshold was noted for F1.

8.2 Rationale

The recurring theme in the behavioral studies reviewed above is that reverberation affects the hearing impaired listener's ability to perceive envelope as well as TFS cues, and that time-varying cues are affected to a greater extent than steady-state stimuli. While there is some neurophysiological evidence regarding the effects of reverberation on envelope and TFS encoding in NH populations, there are no studies examining these effects in the HI population. Further, the FFR has been proven an effective non-invasive window to analyze envelope and TFS cues in reverberant listening conditions in NH subjects. Data from Chapters 4-7 have demonstrated the ability of the FFR to encode envelope and TFS cues in HI subjects Based on the collective findings from behavioral, single-unit and electrophysiological experiments, it is reasonable to hypothesize that the effects of reverberation on subcortical speech encoding may be reflected in the brainstem FFR in HI subjects. The specific objective of the present experiment is to use the FFR to characterize neural encoding of envelope and TFS cues in response to a time-varying speech signal (diphthong) under various conditions of reverberation in NH and HI participants.

8.3 Methods

Please refer to Chapter 3 (General Methods) for specific details of participant profiles, FFR recording protocols and data analysis techniques.

8.3.1 Participants

- Total number of participants: 34 (NH=15, HI=19)

- NH:
    - Clean condition: 15 participants (male=4, female= 11); Age range: 22-32 years (*M*=25.07 years, *S.D.*=2.78 years.
    - In the reverberant conditions: 11 participants (male=4, female=7); Age range= 22-32 (M= 25.09; SD=2.91)
- HI: 11 participants (male=8, female=3); Age range= 22-72 (M= 50.36; SD=17.07)

8.3.2 Stimulus

A synthetically generated, time-varying diphthong /au/ (F0:120-114 Hz, F1:680-440 Hz) was selected as the base stimulus. The stimulus was 150 ms in duration. A dynamic stimulus was chosen for this experiment as time-varying aspects of a signal are affected to a greater extent by reverberation than steady-state signals (Sayles and Winter 2008). The diphthong was generated under three conditions of reverberation (mild, moderate and severe) using a MATLAB algorithm. The methodology for adding reverberation to the stimulus was similar to the procedure described in Bidelman and Krishnan (2010) and Sayles and Winter (2008). Briefly, room impulse responses recorded in a corridor at three distances from a sound source were convolved with the diphthong in the time domain to produce three reverberant conditions: mild, medium and severe. Given below are the distances from the sound source and reverberation times corresponding to each reverberant condition:

- 0.63 m: mild reverberation; Reverberation Time (RT60)~0.7 s)
- 1.25m: medium reverb, RT60~0.8 s
- 5 m (severe reverberation, RT60 0.9 s))

In addition to these three conditions, FFR data was also collected in response to a dry or no reverberation condition. The presentation level of all four stimulus conditions was 80 dB SPL.

8.4 Results

8.4.1 Grand averaged FFRs in NH & HI

Grand averages of the FFR waveform for envelope (FFR_{ENV}) and TFS (FFR_{SPEC}) for the NH and HI groups for the clean and severe reverberation conditions are shown in Figure 8.1. NH FFR response waveform amplitude was greater than the HI response waveform amplitude for both FFR_{ENV} and FFR_{SPEC} for all but the severe reverberation condition, indicating a more robust neural phase-locking mechanism in the NH group than the HI group. In addition, the FFR_{ENV} waveform becomes more robust as reverberation changes from severe to dry in the NH group. Such an effect is not seen in the HI group.

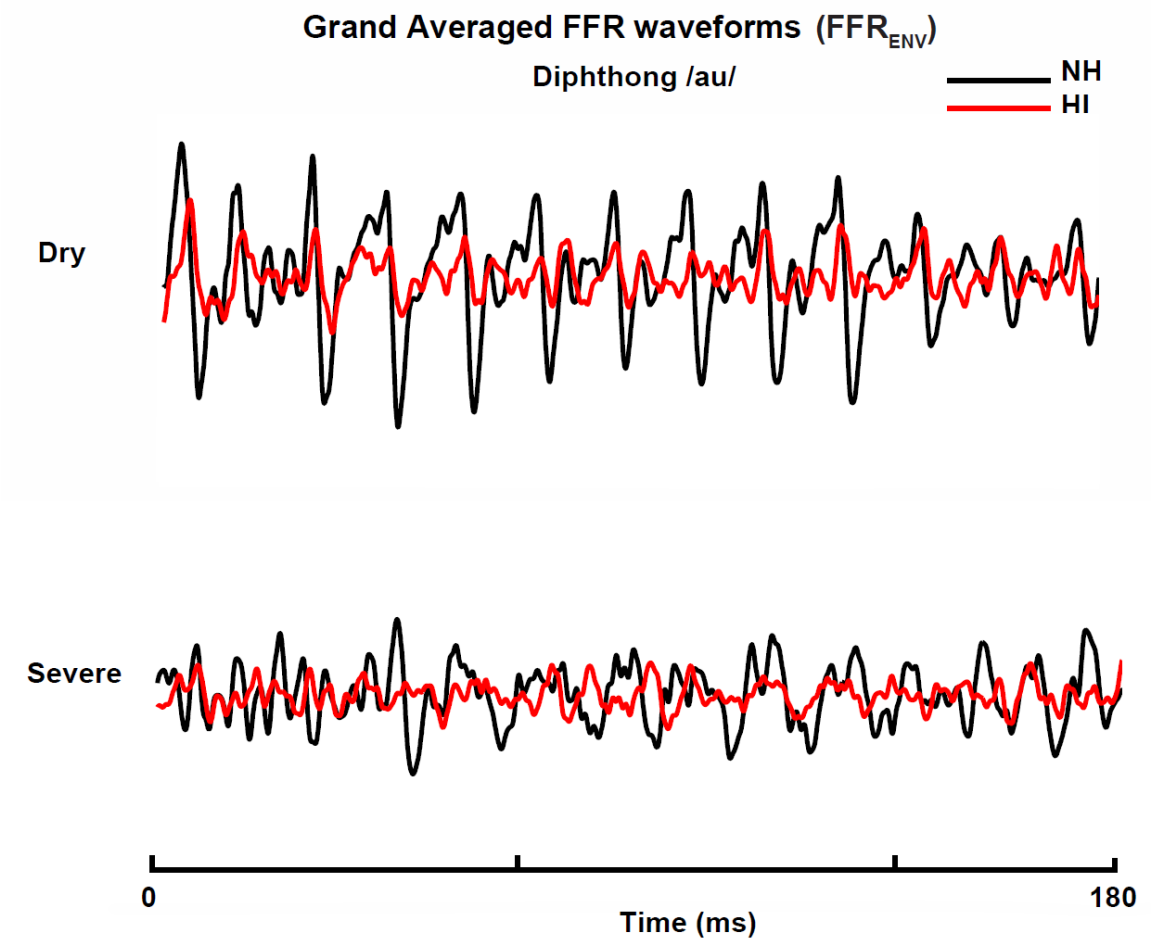

Figure 8.1: Grand averaged FFR waveforms for the envelope condition for the dry condition (top) and severe reverberation (bottom). HI (red) responses are superimposed on NH (black) responses.

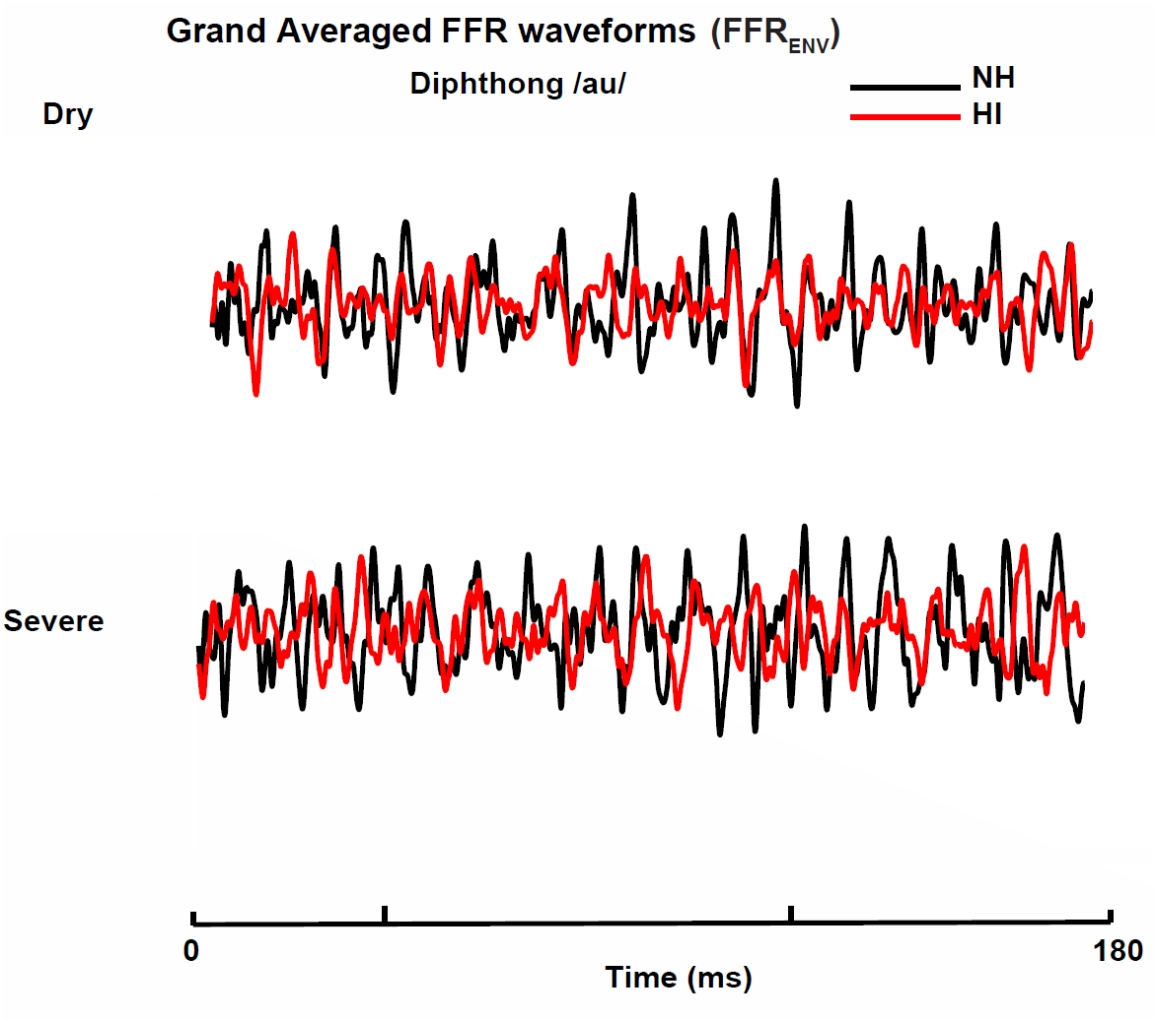

Figure 8.2: Grand averaged FFR waveforms for the spectral condition for the dry condition (top) and severe reverberation (bottom). HI (red) responses are superimposed on NH (black) responses.

8.4.2 Grand averaged spectrograms & correlograms

Grand averaged autocorrelograms of the FFR_{ENV} waveforms derived for NH and HI at each reverberation condition are shown in Figure 8.3. Stronger and clearer bands of phase locked activity are seen at the reciprocal of F0 in correlograms of the NH listeners than the HI listeners in the dry condition. Similarly, stronger (more intense) and precise bands of energy are noted in the NH spectrogram as compared to HI spectrogram at F0 in

the dry condition. Both spectrogram and correlogram bands at F0 and F0-related harmonics become weaker as reverberation increases from mild to severe in both groups

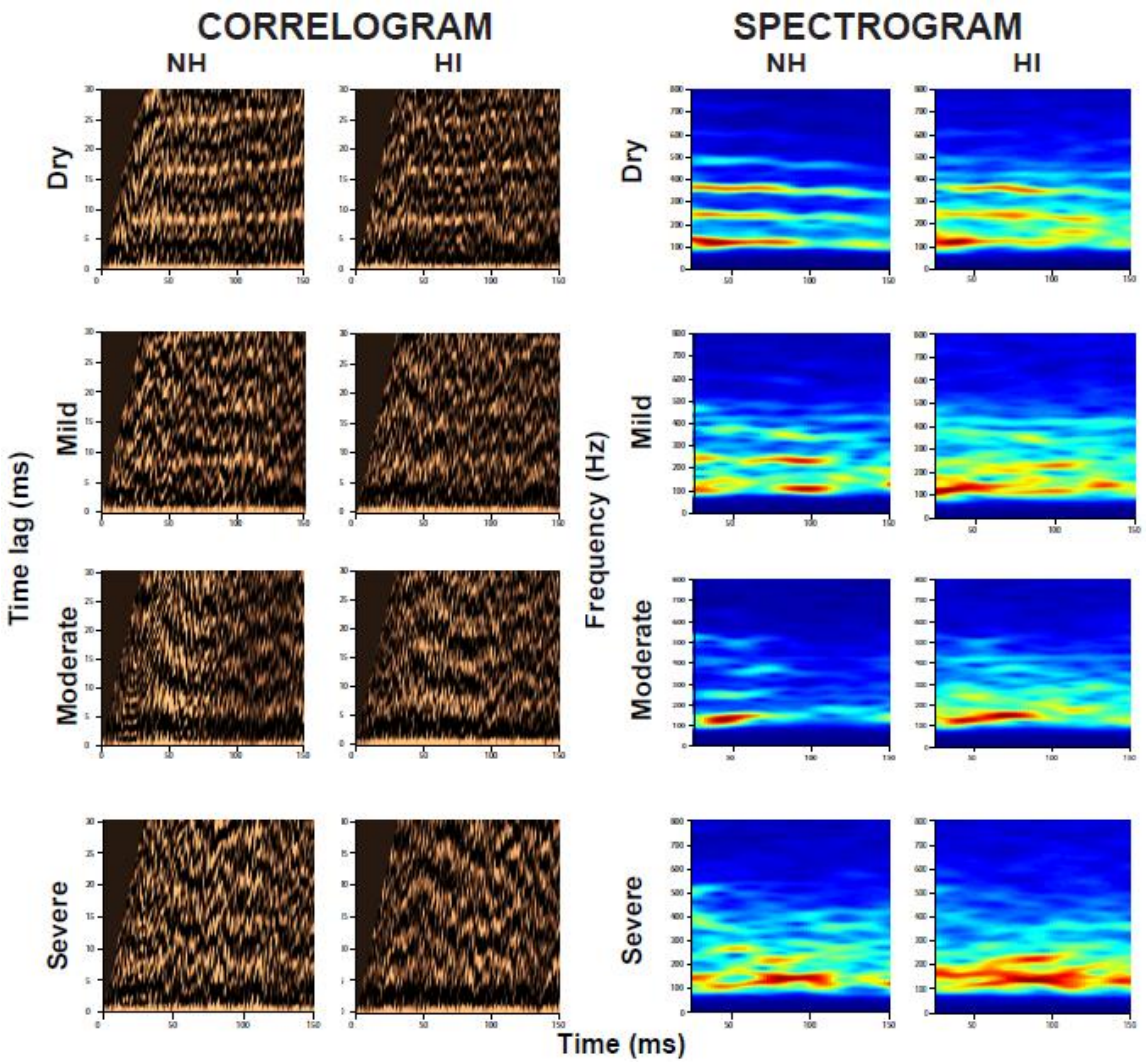

Figure 8.3: Grand averaged correlograms (columns 1-2) and spectrograms (3-4) for NH (cols. 1 & 3) and HI (cols. 2 & 4) at different reverberation levels

8.4.3 FFT & ACF analyses

Grand averaged spectral (FFT) and temporal (ACF) analyses are shown in figures 8.4 and 8.5. It can be seen that F0 representations in the envelope condition are more

resistant to the effects of reverberation, particularly in the NH subjects. On the other hand, formant representation in NH is dramatically reduced with introduction of reverberation. Additionally, group differences between NH and HI are greater for the envelope condition as compared to the spectral condition. For both NH & HI, ACF peaks (figure 8.6) are sharper in the dry condition, as opposed to a much broader peak at the reciprocal of F0 in the reverberant conditions. ACF peaks are greater in magnitude in NH than HI across reverberation condition indicating an effect of hearing impairment.

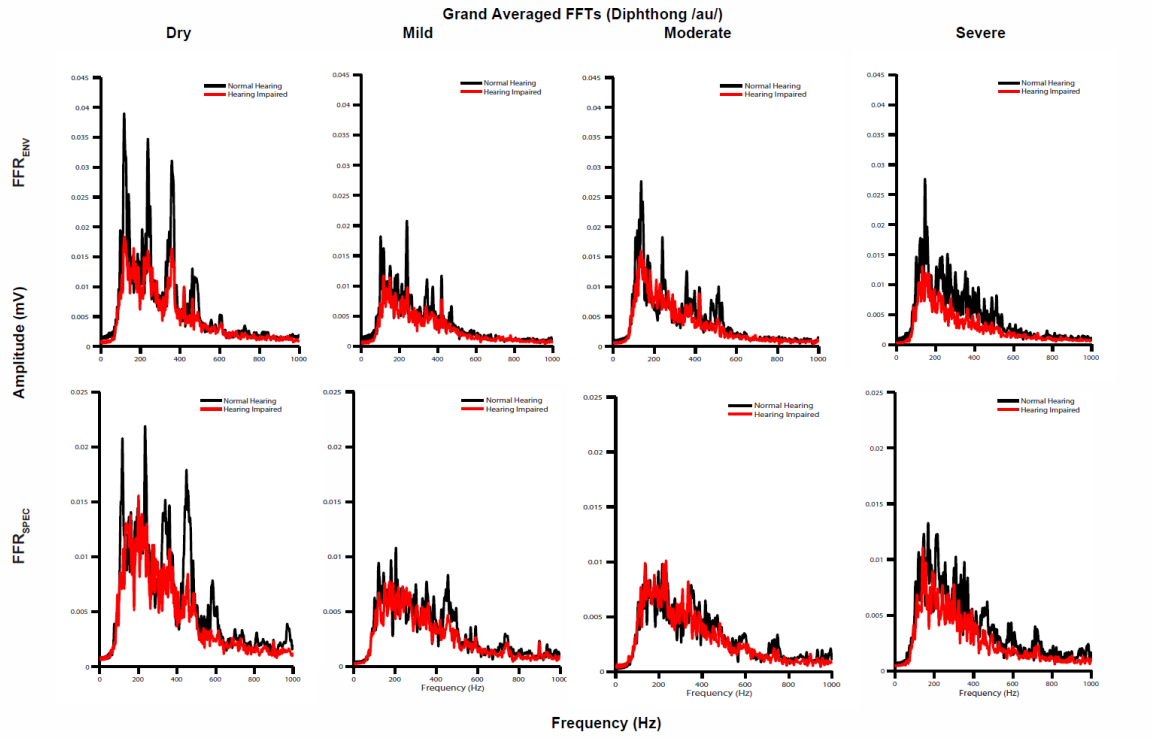

Figure 8.4: Grand averaged FFT responses for the envelope condition (top panel) and spectral condition (bottom panel). HI (red) responses are superimposed on NH (black) responses

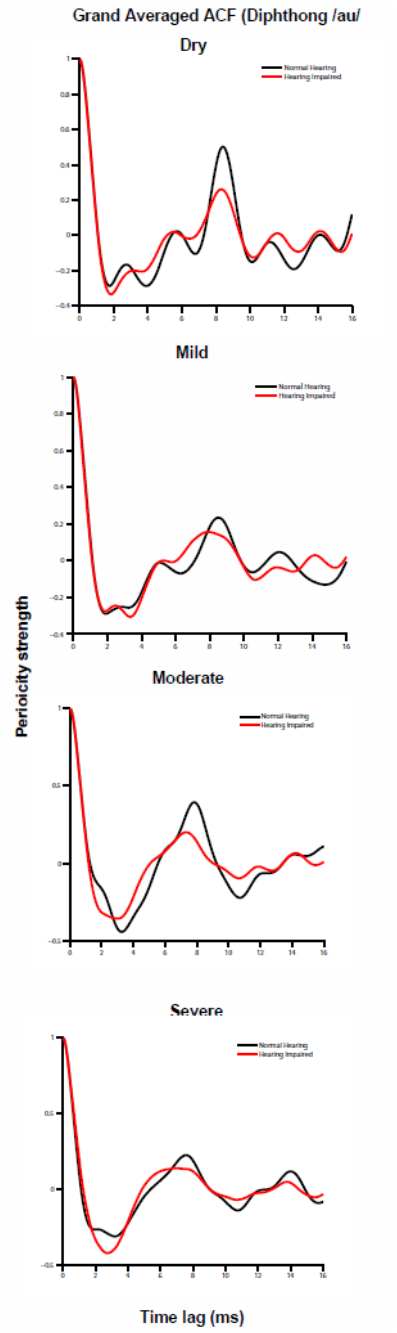

Figure 8. 5: Grand averaged ACFs for the envelope condition for the dry, mild, moderate and severe reverberation conditions. HI (red) responses are superimposed on NH (black) responses

8.4.4 Spectral Correlation

A two way analysis of variance model with group and reverberation condition as the two factors was used to address three primary questions: 1) is subcortical neural encoding different for NH and HI in reverberant listening conditions? 2) Does subcortical neural encoding of envelope and/or TFS encoding change as a function of reverberant condition? 3) Is there an interaction between hearing loss and reverberation condition?

Estimates of neural envelope encoding to the stimulus F0 were obtained for both NH and HI listeners by performing a stimulus-response correlation analysis between the extracted stimulus envelope and the FFR_{ENV} waveforms. The ANOVA yielded significant main effects for hearing loss ($F(1,80)=35.99$, $P<0.0001$), and reverberation ($F(3,80)=3.58$, $P=0.0173$). The interaction effect between hearing loss and reverberation was insignificant ($F(3,80)=2.45$, $p=0.0696$), albeit marginally. Overall these results suggest that F0 magnitudes in NH subjects are greater than those of HI subjects across all levels of reverberation. Post hoc multiple comparisons within the NH group indicated that F0 encoding was degraded significantly only for the most unfavorable condition (dry=mild=moderate > severe). For the HI group, there were no differences in F0 encoding across all reverberation conditions (dry=mild=moderate=severe). In other words, as reverberation increased, a minimal degradation was seen in F0 encoding for NH and none for HI subjects; however, NH subjects had better envelope encoding than HI subjects across all but the most severe reverberant condition.

For FFR_{SPEC}, the two way ANOVA yielded a significant main effect for hearing loss ($F(1,80)=19.23$, $P<0.0001$ and reverberation ($F(3,80)=9.25$, $P<0.0001$). The interaction effect between hearing loss and reverberation was also significant (F

(3,80)=3.37, P=0.02), suggesting that effects of hearing loss on FFR encoding are dependent on the level of reverberation. Least squared means sliced by reverberation condition indicated that NH TFS encoding was greater than HI TFS encoding for the dry (F(3,80)=21.45, P<0.0001) and moderate reverberation (F(3,80)=9.08, P=0.0035)conditions but no differences were seen for the mild (F(3,80)=1.03, P=0.3128) and severe (F(3,80)=0.14, P=0.7086) conditions. Least squared means sliced by hearing loss indicated a significant reverberation effect for the NH group (F(3,80)=13.29, P<0.0001) but not for the HI group (F(3,80)=0.73, P=0.53). In other words, as reverberation increased, significant degradation was seen in F1 encoding for NH and none for HI subjects.

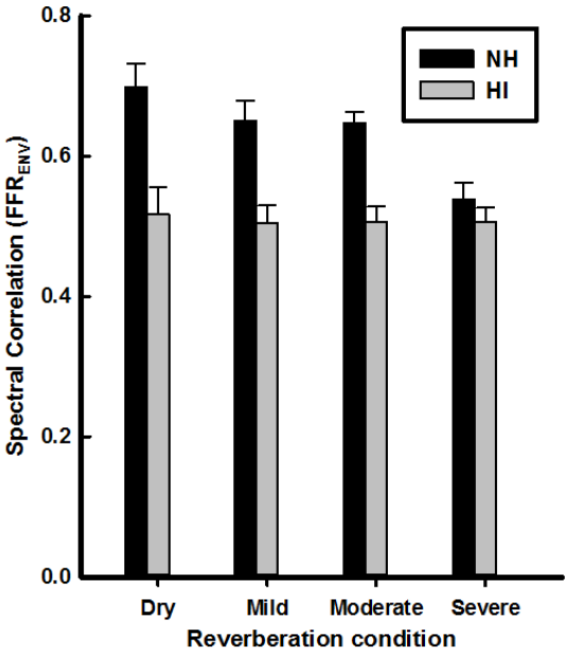

Figure 8.6: Spectral correlation for envelope FFR in NH (black bars) and HI (grey bars) across reverberation levels

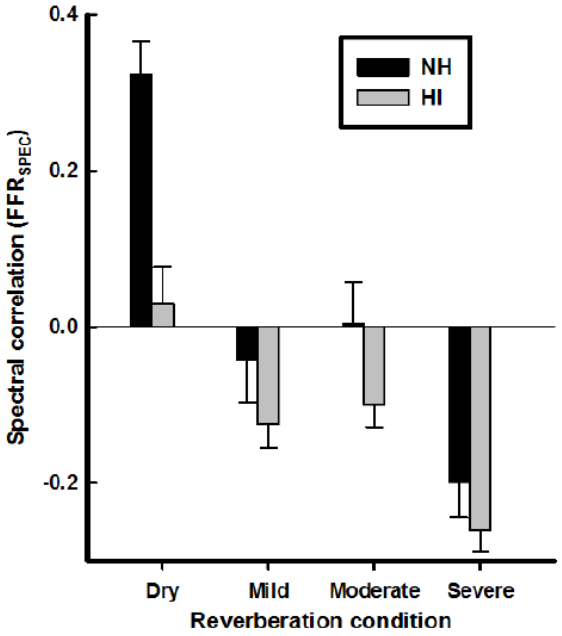

Figure 8.7: Spectral correlation for spectral FFR in NH (black bars) and HI (grey bars) across reverberation levels

8.5 Discussion

FFRs were collected in response to the time-varying diphthong /au/ at four different reverberation conditions: dry (no reverb), mild, medium and severe reverberation. a minimal degradation was seen in F0 and a significant effect for harmonic encoding in NH with reverberation; no reverberation related effects on envelope or TFS encoding were observed for HI subjects. NH subjects had better envelope encoding than HI subjects across all but the most severe reverberant condition. On the other hand, there were no differences between NH and HI subjects for F1 encoding in two out of three reverberant conditions.

Bidelman and Krishnan (2010) noted strong correlations between effects of reverberation on neural encoding and perception of F0 and F1. Perceptual deficits consequent to reverberation are due to spectro-temporal changes such as formant

flattening, self and overlap masking. Hence, reduced neural phase-locking in reverberant conditions may be attributable to spectro-temporal changes in the stimulus subsequent to reverberation.

8.5.1 Effects of reverberation on envelope encoding

Reduction in envelope encoding with increasing reverberation is consistent with findings from neurophysiologic studies such as Bidelman & Krishnan (2010) and Sayles & Winter (2008). Single unit studies have demonstrated that envelope encoding is mediated via phase locking to modulations created by interaction of unresolved harmonics (Cariani & Delgutte, 1996a, 1996b; Meddis & O'Mard, 1997), as have studies of subcortical neural encoding (Greenberg et al., 1987; Smalt et al., 2012). Unresolved harmonics are especially sensitive to reverberation (Sayles & Winter, 2008). Reverberation-induced phase randomizations at unresolved harmonics may explain degraded envelope encoding in NH participants in the current study. Differences in envelope encoding however, were observed to be minimal in the NH group, with the only significant difference occurring between the dry and severe reverberant conditions. These findings are consistent with results from Bidelman and Krishnan (2010), who demonstrated that the effects of reverberation are minimal for neural envelope encoding in the NH FFR.

It is well-established that envelope cues play a major role in pitch perception for HI listeners. The importance of unresolved high frequency harmonics in envelope detection combined with the presence of high frequency hearing loss in most of the HI subjects in the current study explains the difference between NH and HI subjects in the

dry (no reverberation) condition. Such hearing loss related effects on envelope encoding are also noted in FFR data from Chapters 4-7.Based on single-unit findings from Sayles and Winter (2008), it is reasonable to hypothesize that distortion of phase relationships in the unresolved harmonics in reverberation superimposed on the already diminished envelope encoding subsequent to high frequency hearing loss may exacerbate neural envelope encoding in HI subjects. However, although subcortical neural envelope encoding was reduced as compared to NH subjects, there were no changes in neural encoding of envelope cues with reverberation, as observed in the stimulus-response correlations derived from the HI response. These findings are inconsistent with behavioral data which suggests that diphthong perception is affected in reverberation. The lack of a reverberation induced effect in the HI group may also be a consequence of the poor morphology reflecting the combined effects of hearing loss and reverberation. Poor morphology may pose considerable challenges in identifying response components. However, data visualizations using spectrograms, correlograms and autocorrelation functions suggest a definite degradation in F0 encoding as a function of reverberation in HI. This degradation is seen clearly between the "clean" and severe reverberant conditions in the HI group, indexed by smearing of F0-related bands in the spectrograms and a broader peak in the ACF. Hence, it is possible that the traditionally used analysis metrics such as spectral correlations are not sensitive enough to capture the effects of reverberation superimposed on HI effects, owing to highly "noisy" responses in the HI subjects.

8.5.2 Effects of reverberation on TFS encoding

TFS encoding in NH subjects is affected to a greater extent than envelope encoding in reverberation. Again, these results are similar to FFR data from Bidelman & Krishnan (2010), where reverberation induced degradation of F1 related harmonics was noted to be stronger than that of F0. It is possible that such a differential effect is seen in the harmonic FFR data because of relatively greater spectro temporal effects of reverberation in the higher frequencies in the stimulus. The F0 transition in the diphthong stimulus was about 6 Hz (114-120 Hz) whereas the F1 transition was relatively larger at 150 Hz (630-440 Hz). Flattening of formant transitions and differential pitch shifting depending on transition direction are known effects of reverberation. It may be hypothesized that the F0 transition segment in the diphthong used was too narrow to be affected by these spectro-temporal changes as opposed to a sufficiently wider F1 transition. However, the lack of degradation in TFS encoding in HI subjects does not fit in with the above arguments.

Reverberation causes temporal smearing of TFS cues in the resolved region. Numerous studies have established the existence of TFS deficits in hearing impairment. It is then reasonable to predict further degradation of TFS cues when reverberation-induced TFS deficits are superimposed on hearing loss induced TFS deficits. However, as with envelope encoding, no effects of reverberation are seen for FFR harmonic encoding in the HI group using stimulus-response correlations. Again, it is also possible that reverberation-induced changes degrade response morphology to such an extent that it renders identification of response components highly challenging.

Differences between NH and HI are limited to the dry condition and minimized or eliminated in the reverberant conditions. It is possible that reverberation has significantly severe effects on TFS encoding in NH subjects and cannot degrade any further for the HI subjects. Taxing an already impaired system (TFS encoding) with further challenges (reverberation) produces no further additive effects in terms of neural phase-locking.

In Chapter 7, which looked at the effects of noise, differences were observed between NH and HI subjects for all save the most unfavorable condition. However, in the case of reverberation in the present experiment, no differences between NH and HI are seen for *any* reverberant condition for TFS encoding. Such differential effects of noise and reverberation on TFS encoding in NH and HI subjects indicate that effects of reverberation are different from those of noise, and are possibly more severe.

8.5.3 Effects of age

The effect of aging in challenging listening situations is well documented (Pichora-Fuller & Singh, 2006). Nábělek (1988) has shown that elderly listeners have greater difficulty than young adults in speech perception in reverberant settings; however these elderly listeners had mild hearing loss. However, according to Kadsen (1970) differences in perception in reverberation between younger and older adults may simply be reflective of differences in hearing acuity.

The FFR is not sensitive to age effects for low frequency stimuli (<1000 Hz) (Clinard et al., 2010); both F0 and F1 in this experiment were less than 1000 Hz. However Clinard et al. (2010) observed age effects on the FFRs in quiet listening conditions, as opposed to reverberation in the current study.

Based on these collective findings, as age matched controls were not included in the present study, the contribution of age to any degradations in the FFR subsequent to reverberation cannot be ruled out. Inclusion of age-matched controls is essential to tease apart the effects of age, hearing loss and reverberation.

8.6 Conclusion

Like background noise, reverberation is a commonly encountered adverse listening condition that poses significant challenges for HI individuals. The present experiment examines brainstem measures of envelope and TFS under various conditions of reverberation in NH and HI subjects. An understanding of the neural correlates of speech perception deficits in HI is essential in order to design new and improved signal processing strategies in amplification devices to overcome such challenging listening environments. Consistent with behavioral and electrophysiological data, results from this study suggest a differential effect of reverberation on envelope and TFS encoding in NH. Degradation of envelope and TFS in NH is likely due to spectro-temporal smearing consequent to reverberation. Phase randomizations at unresolved harmonics and temporal smearing of resolved harmonics superimposed on the effects of hearing loss may explain degraded envelope and TFS encoding in HI subjects in reverberation. Finally, traditionally used autocorrelation and FFT analyses are not sensitive to SNR/reverberation induced changes in subcortical neural encoding in the HI group; hence alternate measurement techniques must be explored and/or developed.

CHAPTER 9. SOURCES OF VARAITION

9.1 Introduction

9.1.1 Motivation

The effect of hearing impairment on speech perception has been well documented in numerous behavioral studies. Some of these experiments often showed considerable inter-subject variability within the HI group. Such inter-subject variability has been attributed to differences in audiometric thresholds, ability to understand speech-in-noise and age (Summers & Leek, 1998; Glasberg & Moore, 1989; Souza & Boike, 2006). While variability in HI performance has been investigated in behavioral studies, there are no studies reported in the literature that examine neural correlates of variability in hearing impairment. The primary objective of this chapter is to address the sources of variation in subcortical neural encoding of speech sounds in hearing impairment.

Variability in the HI group arises due to several different factors including sensitivity of the audiometric measures to extent of cochlear damage; demographic patterns (e.g. age); and experience-dependent effects (e.g. use of amplification). While it may be possible to reduce the confounding effects of some of these sources of variability by optimizing experimental design, practical constraints related to recruitment of hearing-impaired subjects poses a real challenge. For example, it is possible to segregate HI

subjects on the basis of broad categories (e.g. age range or degree of loss); however, it is difficult to control factors like differences in thresholds within a certain range of hearing loss, etiology of hearing loss, and other co-existing conditions. It should also be noted here that identical audiograms does not necessarily reflect identical extent of cochlear damage. Some of the different factors that may contribute toward the variation in HI subcortical speech encoding are examined in the following section.

9.1.2 Source of variation: Age

Age acts as a common confounding factor in several studies examining differences between NH and HI listeners, as well as within the HI group. For instance, Turner, Chi, & Flock (1999) examined nonsense syllable perception in NH and HI listeners, where the average age for the NH and HI groups were 27 and 56 respectively. Similarly, in a sentence perception study, Healy & Bacon (2003) used NH listeners with an average age of 27 years and HI listeners with an average age of 70 years. It should be noted that Healy and Bacon did include two NH older adults in their study, who performed similarly to younger NH individuals-but two subjects may not offer sufficient statistical power to make a conclusion. Given the extensive literature supporting age-related changes in the auditory system, it is becomes important to tease apart effects related to age and those attributable to hearing loss when there are few age-matched controls. Souza & Boike (2006) acknowledge that while it is ideal, it is typically difficult to find enough age-matched controls when designing an experiment involving HI listeners, particularly with identical audiometric thresholds.

Studies examining the effects of age on speech perception and encoding have yielded mixed results. Presented below are findings from behavioral, electrophysiological, cortical and animal studies that argue for and against the presence of age effects on speech perception and encoding.

9.1.2.1 Differences between NH and HI are due to hearing loss

9.1.2.1.1 Behavioral evidence

According to Humes (1996), a decline in speech perception performance between older and younger listeners is attributable to high frequency hearing loss rather than age. This claim is supported by previous findings (Humes, 1991; Humes & Christopherson, 1991) where age effects were not observed for speech perception in quiet when the older and younger subjects were matched for audiometric thresholds. Similar results were obtained by Takahashi and Bacon (1992), Souza and Turner (1994) and Dubno et al. (1984). Nábělek (1988) investigated effects of hearing loss and age on vowel identification in quiet, noise and reverberation. According to the findings from this study, vowel identification in quiet is correlated with hearing loss but not age. Similarly, Summers and Leek (1998) found was no significant relationship between age and F0 discrimination for synthetic vowels in HI listeners, with age accounting for only 4% of the observed variation. However, age effects were noted in a sentence recognition task conducted as part of the same experiment.

9.1.2.1.2 Electrophysiological evidence

Behavioral experiments run the risk of tapping into non-auditory processes such as cognition and memory, which conflate findings in studies where the primary question

of interest revolves around auditory capabilities alone. Physiological experiments which examine pre-attentive sensory level processing, on the other hand, provide the ability to control for such non-auditory processes and reflect solely auditory processing. Boettcher, Poth, Mills & Dubno (2001) found no effects of aging on amplitude modulated frequency response (AMFR) amplitudes and phase, regardless of carrier frequency or modulation depth in young and old subjects with NH. On the other hand, a definite reduction in AMFR amplitude was observed in both older subjects with high frequency hearing loss and younger NH subjects listening with a high pass masker, as opposed to young NH subjects. These results suggest that any reductions in AMFR amplitude seen in older subjects were related to hearing loss and not age.

9.1.2.2 Differences between NH and HI are due to age *and* hearing loss

9.1.2.2.1 Behavioral evidence

Dubno and Dirks (1984) found a significant effect of age on speech recognition in the presence of background noise. These age effects persisted in both NH and HI groups, suggesting that speech understanding in HI in background noise is not a sole function of audiometric threshold, but also age. According to Souza and Boike (2006), age is a strong predictor of temporal processing in hearing impairment. Gordon-Salant, Yeni-Komshian, Fitzgibbons & Barrett, (2006) obtained mixed results when attempting to characterize age-related deficits in natural speech in age-matched NH and HI subjects. An effect of age was noted for identification of the word pairs that varied with respect to temporal features related to consonant manner of articulation, but was not observed for the

discrimination tasks. An effect of hearing loss was noted in the discrimination tasks, likely attributable to loss of audibility, especially at higher frequencies.

9.1.2.2.2 Electrophysiologic evidence

Purcell, John, Schneider & Picton (2004) found a modulation frequency dependent age effect for the envelope following response. Specifically, no differences were observed for the EFR in the performance of the younger and older adults at modulation frequencies between 30-50 Hz, consistent with previous work by Boettcher et al. (2001). At modulation frequencies above 100 Hz, elderly listeners had smaller amplitude EFRs than younger listeners. While this result may reflect an age-related decline in temporal processing abilities at higher modulation frequencies, it is to be noted that the older and younger adults were not matched for audiometric thresholds. The authors acknowledge this in their discussion of the results, but also observe that the EFR and audiometric thresholds were not strongly correlated, thus pointing to a more age-related decline as the interpretation. Leigh-Paffenroth and Fowler (2006) found that amplitude of the AM ASSR declines as a function of age. The results from this study are in contrast with findings from Boettcher et al. (2001), but are confounded by the significant difference between the audiometric thresholds between younger and older adults included in this study.

Grose, Mamo and Hall (2009) studied age effects on temporal envelope processing at two modulation rates (32 Hz and 128 Hz) for two different carrier frequencies (500 Hz and 2000 Hz). These modulation rates and carrier frequencies were selected in order to compare results to findings from previous studies, which have

employed similar modulation rates (Boettcher et al., 2001; Purcell et al., 2004; Leigh-Paffenroth & Fowler, 2006). The results from this study suggest that age effects are seen at higher modulation rates as compared to lower modulation rates, leading to the conclusion that temporal processing at higher envelope frequencies is affected as age increases.

Parthasarathy, Cunningham and Bartlett (2010) examined age-related changes in AMFRs to SAM tones in quiet, noise and at different presentation levels. TMTFs obtained in response to stimuli in quiet were similar at modulation frequencies between 181-512 Hz in both young and aged populations, as was the growth in AMFR amplitudes as a function of stimulus presentation level. However, significant group differences were noted in the TMTFs as background noise was introduced with the SAM tones. The authors hypothesized that these observed age effects may be related to reduced inhibitory mechanisms in the aging auditory system. In a follow up study, Parthasarathy and Bartlett (2011) found significant differences in AMFRs and FMFRs in young and old rats at reduced modulation depths and complex envelope shapes. These differences were not seen when the modulation depth was high or the envelope was unaltered (as in Parthasarathy et al. (2010), suggesting that temporal processing is more susceptible to age effects when the stimuli are complex.

Cortical temporal processing measured by P1-N1-P2 latencies in young and old NH adults in response to CV stimuli with varying VOT indicates delayed N1 latencies (for VOTs > 30 ms) in elderly NH individuals (Tremblay, Piskosz, & Souza, 2002). Hence, older adults may have deficits in temporal processing due to disruptions/delays in

neural synchrony. These deficits may be exacerbated in the case of hearing loss. Tremblay, Piskosz and Souza (2003) studied cortical temporal processing in older HI subjects in addition to young and old NH adults, and found enhanced N1 amplitudes in the HI subjects, inconsistent with established literature. Tremblay et al. (2003) discuss the challenges involved in isolating age and HI-related effects within the HI population. They concluded that a combination of both age and hearing loss may be contributing towards the observed results in the HI population.

9.1.2.2.3 Subcortical evidence:

The auditory brainstem response (an onset response) has demonstrated decreased neural synchrony with increasing age in NH individuals, reflecting age-related effects on subcortical neural encoding. However, there are no studies reported in the literature that have examined the effects of age *and* hearing loss at the subcortical level using the FFR. Clinard et al. (2010) used the FFR to study in greater detail the effect of age on neural phase locking to tone burst stimuli grouped around 500 and 1000 Hz in NH subjects. FFR measures of amplitude and phase coherence derived from the FFT declined with age only for the higher frequency tone burst centered around 1000 Hz, while no age-related changes were seen at 500 Hz. In other words, the subcortical sustained physiological representation is frequency dependent. Clinard et al. (2010) infer that the upper limit of phase locking may be affected by age, thus explaining why the response at 1000 Hz is affected whereas the FFR at 500 Hz remains largely unaffected with age. Interestingly, the authors found significant age effects at both 500 and 1000 Hz in a behavioral task

using the same stimuli, indicating a dissociation between the neural and behavioral metrics measuring age-effects.

In summary, age effects in hearing impairment are variable, and depend to a great extent on the stimulus complexity and listening background.

9.1.3 Source of variation: Audiometric thresholds:

Audiometric thresholds can account for some portion of the variability in HI performance. As part of a larger experiment, Summers and Leek (1998) compared F0 DLs for five steady-state vowels in NH and HI listeners. The steady state vowels used in this study were similar to those used in the current experiment, having time-invariant F0s at 120 Hz with a duration of 260 ms. 3/7 HI subjects showed F0 DLs comparable with NH subjects; one subject showed borderline performance and the remaining three HI subjects showed significantly increased F0 DLs. Correlating F0 DL performance with audiometric thresholds using a stepwise regression model, Summers and Leek (1998) found that the audiometric threshold at 2000 Hz accounted for a major portion of the variance in F0 discrimination thresholds. On the other hand, there was no significant relationship between age accounted for only 4% of the variation in the F0 DL.

9.1.4 Source of variation: neural plasticity

Neural plasticity is a commonly used umbrella term for a variety of physiological/anatomical changes that take place in the neuronal units of the brain and brainstem. With respect to hearing loss and the auditory system, rewiring of neurons may

be broadly classified into three major categories: plasticity induced by reduced auditory input due to signal attenuation and distortion consequent to hearing loss, neuronal reorganization facilitated by the use of amplification; exposure to auditory signals, and neuronal reorganization caused by learning processes before or after hearing aid use (Williott, 1981). Neural plasticity can occur at all levels in the auditory system. Specific plastic changes may include rewiring of tonotopic maps, reorganization of spatial maps that determine directional hearing and hearing in noise; and changes in synaptic activity patterns.

Tonotopicity in the auditory system is well established at all levels starting from the cochlea to the auditory cortex. Evidence from animal models has shown that frequency maps may be changed with hearing loss when healthy regions of the cochlea "take over" functioning of the damaged portions. Measurements of tuning curves made in mice with high frequency hearing loss have revealed significant tonotopic remapping (Willott 1984, 1986; Willott Parham Hunter, 1988, Willott Aitken McFadden 1993). A loss of sensitivity at high frequencies renders neurons with high frequency CFs unresponsive. With high frequency hearing loss, there is a loss of tuning in the high frequency region of the IC, with the typical steep low frequency tails of a high CF fiber flattening out. As a result, thresholds for low frequency tones change from as high as 80 dB SPL to as low as 60 dB SPL. Thus, there is greater contribution from the cochlear apex indicating tonotopic remapping. Tonotopic remapping in high frequency hearing loss, in both the IC and the auditory cortex, causes a shift in neurons with high CFs (>20 kHz) towards middle frequencies (10-15 kHz), which shift to even lower frequencies when hearing loss extends towards the middle frequencies. Hearing loss related plasticity

has differential effects at different points in the auditory system, with greatest effects evident at higher levels (cortex) and lesser at lower levels (cochlear nucleus).

When neurons on adjacent healthy portions of the basilar membrane start "covering for" neurons in damaged regions, normal neural encoding is disrupted due to excess neuronal excitation for certain stimuli. Neural representations of pitch may also be distorted if plasticity effects cause a remapping of the basilar membrane.

Spatial maps that determine binaural hearing, hearing in noise, localization and lateralization are often reorganized in hearing loss. Such reorganization is often seen following unilateral hearing loss or unilateral amplification of a bilateral hearing loss, which causes an imbalance in the input at the two ears. Binaural processing is likely altered because of imbalances in excitatory and inhibitory mechanisms in hearing loss.

Muscles have been found to have increased excitatory responses and sensitivity to neurotransmitters, as well as undergo physiological changes following reduced synaptic input in disuse (Kuffler, Nicholls and Martin, 1984). Similarly, reduced synaptic input in hearing loss also causes anatomical (neuronal shrinkage, atrophy) and physiological changes (changes in spontaneous activity, loss of inhibition in the IC and altered tuning curves).

Plasticity can also occur as a result of exposure to auditory stimuli. Clopton and Winfield (1976) and Poon and Chen (1992) found improved IC responses to tonal stimuli in rats who had been exposed to these sounds for considerable portions of time into their young adulthood. Shanes and Constatntine-Paton (1983) who found broader tuning curves in the IC of mice that had been exposed to clicks (broad spectrum). While such neural reorganization has been documented in immature animals, experience-dependent

plasticity is also evidenced in adulthood, as demonstrated by different synapses in adult rats exposed to tonal stimuli as compared to un-exposed rats. Experience-dependent plasticity has also been documented at the level of the brainstem in humans using the FFR (discussed ahead).

Conditioning paradigms can also cause neural remapping in the auditory system. Repeated association between a stimulus and a consequence causes changes in synaptic strength in some neural circuits. Auditory conditioning paradigms typically cause an increase in neural responses at both cortical and subcortical levels; such plasticity can be rapid. Weinberger (1995) showed a conditioning associated shift in neuronal BF from the frequency of the conditioned stimulus, when the conditioned stimulus was paired with a shock in adult rats.

Evidence from subcortical studies suggests that pitch preservation and encoding is strongly shaped by experience-dependent learning effects. Krishnan, Gandour and Bidelman (2012) provide an excellent review of subcortical studies investigating neural plasticity with respect to language and music. Brainstem pitch representation of time varying stimuli (e.g. Mandarin tones) native to speakers of tonal languages (e.g. Chinese) has been found to be more robust in tone-language speakers (Chinese speakers) as compared to speakers of non-tonal languages (e.g. English); these differences persist when the stimulus is degraded. When musically relevant signals are presented, subcortical neural encoding is more robust in musicians as compared to non-musicians. Interestingly, cross-domain studies of music and language have results indicated that experience-dependent effects are not specific to a particular domain but are transferrable across areas. Stronger subcortical neural encoding has been documented in English

musicians as compared to English non-musicians in response to Mandarin tones. Similarly, Chinese speakers demonstrate enhanced subcortical encoding as compared to English non-musicians in response to stimuli containing musical pitch intervals.

Further, FFRs have been shown to improve in F0 encoding subsequent to speech-in-noise perception training in NH young adults (Song et al., 2006). Increases in subcortical encoding of F0 have also been noted in young adults who have completed 20 hours of training on the LACE (Song et al., 2006). Additionally F0 amplitude prior to auditory training served as a good predictor of training-induced change in subcortical speech encoding.

Overall, experience-dependent neural plasticity effects have direct implications for secondary plasticity arising from the use of amplification. Electrical stimulation of IC neurons in deafened cats indicates changes in IC tonotopicity (Snyder, Rebscher, Cao, Leake & Kelly, 1990), suggesting that plasticity effects following reintroduction of sounds do occur in an impaired auditory system. Secondary plasticity may be complicated (or enhanced) by initial plasticity changes that might have occurred as a result of hearing loss. Gaining a strong handle on the effects of secondary plasticity and interaction of plasticity effects induced by hearing loss, experience and conditioning is essential in understanding and predicting benefit from amplification and auditory training.

9.2 Rationale

In the current study, a majority of the participants in the NH group consisted of graduate and undergraduate students recruited from the Purdue University campus. Hence, the general make-up of the NH group was fairly homogenous in terms of

audiometric thresholds and age. However, the HI group included participants spanning a wide age range of audiological profiles. While all the HI participants had hearing thresholds in the mild to moderately severe range, they differed in terms of age, audiometric thresholds across frequencies, age of onset of hearing loss, duration of hearing loss, use of hearing aids, satisfaction with hearing aids, music experience. Studies have found that speech perception in HI listeners is affected by age and degree of hearing loss (see Gordon-Salant, 2005; Pichora-Fuller & Singh, 2006 for a complete review). Several studies have demonstrated changes in neural circuitry subsequent to hearing loss and hearing aid use (Dietrich, Nieschalk, Stoll, Rajan, & Pantev, 2001; Korczak, Kurtzberg, & Stapells, 2005; Oates, Kurtzberg, & Stapells, 2002; Syka, 2002). Based on these findings, it is not unreasonable to expect that the variability in the HI FFR data may also reflect the effects of one, or a combination, of these sources of variability. Hence, it is important to gain a better understanding of the characteristics of this variability in order to minimize its confounding influence. This is also essential in order to use the FFR measure as an effective diagnostic tool to characterize neural encoding in HI subjects, as it may enable predictions on benefit from amplification and/or auditory training while taking into account the effects of age and hearing loss. The aim of this chapter is to isolate the possible sources of variation in neural encoding of speech, and to discuss potential clinical implications of such variation.

9.3 Methods and Results:

A detailed audiological and medical case history was completed for each HI subject. The participants with hearing impairment had varying audiological case histories,

differing in terms of etiology of hearing loss, age of onset of hearing loss, duration of hearing loss, use of amplification, duration of amplification and satisfaction and benefit from amplification.

A multiple regression procedure was used to analyze the relationship between the dependent variables (subcortical envelope encoding, subcortical TFS encoding) and the predictor variables (age, low frequency pure tone average, high frequency pure tone average, hearing aid use, hearing aid satisfaction and music experience). As this was an exploratory analysis, the use of the "all possible subsets" approach determined the best model using an optimum number of predictor variables based on adjusted R-squared and Cp values. All nineteen HI subjects were included in the analysis. Based on adjusted R-squared and Cp values, the best model explaining the relationship between FFR F0 encoding and the predictor variables included predictor variables low and high frequency pure tone average, hearing aid satisfaction and music experience.

Recall from Chapter 4 that the HI group was separated into strong and weak performers using a cluster analysis. As findings from the current experiment identify possible sources of variation, it is of interest to analyze the profiles of the five high performing HI listeners systematically with respect to age, degree of hearing loss, hearing aid use, hearing aid satisfaction, music experience to identify any characteristics that may explain why their FFR is comparatively stronger. The use of a stepwise multiple regression model would have been ideal; however, it was rendered mathematically impossible as the number of variables were greater than the number of subjects available for analysis (n=5). Hence, while a statistical analysis was not possible due to the low number of subjects, the data are described qualitatively.

- Age: There were 5 subjects below 40 years in the entire HI population (n=19). Of the entire HI population under 40, there was only one subject (age: 22 years) who was included in the high performing group.
- Hearing aid use: 11/19 HI subjects reported having used hearing aids at some point in their lives. 3/5 (60%) high performing HI subjects who had strong subcortical envelope encoding were hearing aid users.
- Hearing aid satisfaction: 6/11 hearing aid users reported satisfaction with their amplification devices. 3/5 (60%) high performing HI subjects who had strong subcortical envelope encoding were satisfied with their hearing aids.
- Therefore, all hearing aid users who had strong subcortical encoding (3/3=100%) reported satisfaction with their devices.
- Music experience: 2/5 high performing HI subjects reported music experience (40%).

Overall, these results are difficult to interpret because 1) there are only five high performing HI subjects 2) there is considerable overlap between the five subjects in terms of the predictor variables. For example, all three hearing aid users with strong subcortical envelope encoding were also satisfied with their devices. Therefore, it is difficult to pinpoint one single reason for their high performance. A systematic evaluation of each of these variables of interest while controlling for the remaining is required before conclusions can be made about contributions from any variable. For e.g., to study the effects of music experience on the HI FFR, the only difference in the test and control HI groups must be in terms of music experience. The test and control HI subjects must be

homogenous in all other respects such as audiometric threshold, age, etc. However, as discussed in Section1, it is highly challenging to achieve such homogeneity with a typical representative human HI sample.

9.4 Discussion:

The role of audiometric thresholds as a source of variability in the FFR is not unexpected. NH and HI listeners were so divided on the basis of their audiometric thresholds, and show significant group differences. Behavioral studies (Summers & Leek, 1998) have established that F0 discrimination in HI listeners is best correlated with their audiometric threshold at 2kHz. Hence, inclusion of audiometric threshold as a source of variability in neural encoding of speech is consistent with established behavioral literature.

Music experience was included in the best model predicting subcortical envelope encoding; while this has the potential to be an interesting result, it should be interpreted with caution. Music experience-dependent effects were not the primary focus of the present study; hence there were no established guidelines that were applied to segregate musicians from non-musicians (e.g. number of years of training). Those classified as has having music experience in this study reported having formal music training *at some point* in their lives.

However, given the experience-dependent plasticity effects observed in the FFR subsequent to music training in NH listeners, it is not unreasonable to suggest that such effects may be seen in HI listeners as well. Could the enhanced subcortical envelope encoding to a speech stimulus in HI participants with music experience be attributable to

experience-dependent learning effects of music? Music experience related learning effects could translate to enhanced subcortical speech encoding in musicians as compared to non-musicians (Musacchia, Sams, Skoe & Kraus, 2007). Bidelman and Krishnan (2010) demonstrated enhanced subcortical speech encoding in musicians compared to non-musicians under various conditions of reverberations. Based on the above evidence, it is certainly plausible that music experience might contribute towards robust subcortical speech encoding in HI individuals. However, this reasoning cannot be extended to the present data as music experience was not a carefully controlled variable in the current study.

Hearing aid use and satisfaction were the other two predictor variables selected by the model. Based on findings by Song et al., (2006) that auditory training can enhance F0 representations in the FFR, it is possible that "secondary plasticity" following amplification could enhance brainstem representations of pitch. Findings that hearing aid usage and satisfaction may improve FFR encoding strength brings up an interesting question: Do HI individuals have stronger pitch encoding mechanisms as reflected in the FFR because of top down effects from hearing aid satisfaction? Or are they satisfied with their hearing aids because they have comparatively stronger pitch encoding mechanisms as indexed by their stronger FFRs? Answers to these questions may lie in a theoretical model of experience-dependent neural plasticity discussed by Krishnan et al. (2012). This model involves local (pitch mechanisms in the inferior colliculus and auditory cortex), and feed-forward (colliculo-thalamo-cortical) as well as feedback (cortico-collicular pathway and cortico-thalamic) loops. According to this model, feed forward and feedback loops activated by functionally relevant signals reorganize plastic pitch

mechanisms in the IC and auditory cortex. Plasticity induced reorganization is subsequently regulated by excitatory and inhibitory mechanisms. It is possible that such a feedback loop may be activated with hearing aid use or auditory training, causing a gradual tuning of brainstem pitch encoding in the amplified system. Once subcortical reorganization occurs, it is maintained through the balance of excitatory and inhibitory mechanisms. This maintenance of subcortical reorganization may be reflected as hearing aid satisfaction. However, the effects of HI-induced plasticity, and its interactions with secondary plasticity (which are presently unknown) must be taken into account when applying the theoretical model of experience-dependent plasticity to hearing loss.

Based on the results from the current investigation, it can only be concluded that subcortical neural representations of speech are affected by a complex interaction between audiometric patterns and experience-dependent effects, the individual roles of which are difficult to tease apart. Understanding the independent role of each of these sources of variation has direct implications for clinical audiology as predictors for benefit from amplification and auditory training and as an objective counseling tool

.

CHAPTER 10. CONCLUSIONS

10.1 Summary of results

The overall objective of this dissertation was to characterize subcortical encoding of speech signals in hearing impairment using an objective electrophysiological neural index, the FFR. Stimulus complexity and listening conditions were systematically varied to provide neural representations of speech encoding in various real-world situations. All FFR recordings obtained in HI participants were contrasted against a NH control group. Chapter 4 demonstrates that the FFR is a viable technique for indexing brainstem encoding of envelope related and temporal fine structure related cues in HI subjects. A key finding is that both envelope-related and TFS-related cues are degraded in subcortical representations of steady state speech sounds in HI participants as compared to NH participants. Degradation in subcortical representation of TFS reflects established findings in behavioral and animal physiology studies, which indicate that TFS cues, crucial for speech perception, are poorly encoded in hearing impairment. Reduced envelope encoding indexed by the brainstem FFR in HI participants is not entirely consistent the popular notion that envelope encoding is equivalent or enhanced subsequent to SNHL, as compared to NH listeners. Numerous factors may account for the differences observed in subcortical neural encoding in NH and HI, which may be classified as “audibility effects” and “distortion related” (degraded neural phase locking

subsequent to reduced frequency selectivity, impaired temporal synchrony and distorted phase responses in unresolved regions involving higher harmonics, amongst others). Aging effects, that may confound effects of hearing impairment, were ruled out using age matched subjects and statistical measures.

The key message from Chapter 4: *subcortical neural representation of speech is degraded in SNHL*.

Audibility effects were tested in Chapter 5 by comparing subcortical encoding in NH and HI for stimuli at presented at equalized audibility based on pure tone averages. Results indicated that access to audibility minimized effects due to hearing impairment, more so for brainstem envelope rather than TFS encoding. Brainstem FFR-intensity level functions suggest possible enhancements in envelope encoding as a function of stimulus presentation-level, similar to recruitment-based enhancements seen in TMTFs of HI listeners. However, weak deficits for envelope encoding and significant deficits for temporal fine structure encoding continued to be seen in HI subjects even with access to audibility, suggesting the role of alternate "distortion" mechanisms. It is possible that the balance between audibility and distortion may be different for different HI subjects. In other words, certain HI participants may perform on par with NH listeners when audibility is restored; such subjects may also perform well with amplification and report more hearing aid satisfaction. On the other hand, subjects with similar audiometric thresholds who continue to show deficits in neural encoding even after access to audibility, possibly indicate a tilt towards "distortion" effects. Such distortion effects may also be manifested as a lack of benefit from amplification.

Thus, Chapter 5 suggests that *degraded subcortical neural representations of speech in hearing impairment cannot be completely accounted for by audibility; rather, these representations reflect a complex interplay of attenuation and distortion effects subsequent to SNHL*.

Everyday speech is rarely steady state; rather, speech is a complex, dynamic signal employing varying temporal, loudness and frequency patterns. In order to index the effects of stimulus complexity and context effects on subcortical representations of speech, Chapter 6 discusses the changes in subcortical encoding in NH and HI subjects as a function of pitch contour (steady-state vs. time-varying) and formant structure (vowel vs. complex tone). Overall, neural representation of the vowel stimulus is more robust than that of the complex tone in NH. Additionally, a dichotomy in neural processing of "source" (envelope related cues) and "filter" (spectral cues) may be inferred from comparisons between FFRs evoked by the vowel vs. the complex tone. The effects of hearing impairment negate the neural encoding advantage for vowel stimulus over the complex tone. Further, results from Chapter 6 establish a robust effect of pitch complexity; in other words, steady-state stimuli are processed more efficiently than time-varying stimuli at the level of the brainstem for both NH and HI participants. This is not to say that time-varying pitch is not encoded robustly; diphthongs were successfully recorded to both NH and HI subjects in the present experiment. Also, HI brainstem encoding may reflect added effects such as reduced frequency selectivity, which may cause further reductions in subcortical encoding of time-varying stimuli. Hence, in terms of clinical application, these findings suggest the use of ecologically relevant (speech)

stimuli that have relatively simple pitch to optimize brainstem pitch encoding measurements in HI participants.

Overall, results from Chapter 6 suggest that *subcortical neural speech encoding is influenced by pitch contour and formant structure in both NH and HI individuals*.

In the real world, speech perception rarely occurs in quiet settings. Chapters 7 and 8 consider the effects of different challenging conditions such as background noise and reverberation on subcortical neural representations of speech. Effects of reverberation and background noise have deleterious and different effects on brainstem speech representations, consistent with behavioral findings. Background noise caused a decrease in both envelope and TFS related cues, whereas reverberation-induced degradations were more pronounced for TFS cues as compared to envelope cues in NH subjects. Numerous effects such as masking, loss of spectral contrast and introduction of spurious peaks occur in reverberation and noise; these effects are exacerbated in HI listeners who already have degraded neural representations of speech. While clear degradations with hearing impairment were observed in spectro-temporal visualizations (spectrograms and correlograms), these degradations were not picked up by autocorrelation, FFT or spectral correlation techniques. It is possible that degradations such as noise and reverberation superimposed on effects of hearing impairment exacerbate neural encoding of speech, producing weak and diffuse patterns of phase locking to spurious peaks of energy unrelated to stimulus-relevant features. As a result, traditional analysis methods are not able to extract any useful information from these responses. Quantifying the effects of degraded listening conditions in hearing impairment is a critical part of understanding subcortical encoding to speech in real world situations. Hence, it is important that

alternate analysis methods (e.g. spectrogram measurements) are developed to study neural phase locking in degraded conditions.

Findings from Chapters 7 and 8 can be summarized as *subcortical neural representations of speech are exacerbated in degraded listening conditions*.

The experiments described thus far were primarily interested in addressing effects of hearing impairment on neural representation of speech, but did not address the variability within the HI group. Chapter 4 identified a group of high performing HI individuals, whose neural encoding strength was similar to average NH neural encoding strength. Prompted by this observation, Chapter 9 provides a detailed analysis of audiological, demographical and experience dependent effects, which may predict brainstem speech encoding. Interestingly, the factors that acted as the best predictors of brainstem neural encoding for the HI group were the degree of hearing loss, hearing aid satisfaction and music experience. That degree of hearing loss is a strong predictor of HI neural speech encoding strength is not unexpected, given that differences between NH and HI FFRs are based, at least overtly, on the degree of hearing loss. However, findings that hearing aid satisfaction and music experience contribute towards FFR representations in hearing impairment have strong implications for clinical audiology. Experience dependent learning effects are known to fine tune and enhance pitch representations in the FFR through colliculo-thalamo-cortical, cortico-collicular and cortico-thalamic feedback loops. Such experience dependent learning effects have also been shown to extend across the domain of expertise. It is possible that long-term effects of musical training causing subcortical reorganization in HI systems manifest themselves in brainstem representations of speech. Further, and even more exciting in terms of clinical

audiological applications, is the reflection of hearing aid use and satisfaction in brainstem representations of pitch, which may be indicative of top-down modulation effects. If true, the FFR may be an excellent non-invasive and objective measure of hearing aid benefit and/or auditory training. However, it may be presumptuous to make these claims, as the effects of various predictors may overlap (e.g. satisfied hearing aid user and several years of musical experience) in the HI participants in the present of experiments. Further systematic investigations within HI listeners with well-matched controls for each of these audiological, demographical and experience-dependent factors are required before any conclusions regarding plasticity-induced effects in HI subcortical encoding can be made.

The take-home message from Chapter 9 is that *subcortical neural representations of hearing impairment may be predicted by certain audiological or experience dependent effects; if true, this finding would have major clinical implications*.

10.2 Role for the FFR in the Audiology Clinic

The FFR has tremendous potential as a clinical tool in audiology clinics. Firstly, it is a reliable, objective and non-invasive measure that is supported by close to five decades of research. The FFR set-up is similar to that of the ABR and can be recorded when the subject is asleep. These characteristics of the FFR make it a viable test for use with infants, young children and difficult to test populations. Further, the FFR provides a robust measurement of subcortical speech encoding, and can be recorded in response to a plethora of stimuli. The FFR is known to index neural plasticity, and has been used to demonstrate differences in pitch encoding skills of various clinical populations such as specific language impairment and dyslexia. Given the response profile of the FFR, it can

potentially be developed as a reliable tool for hearing aid fitting and monitoring benefit from amplification and/or auditory training. Hearing aid fitting in infants and young children is based largely on the auditory brainstem response or the auditory steady state response, both well-established electrophysiological measures. However, neither of these measures provides information about speech encoding at the level of detail that the FFR does. The FFR has the ability to represent several important acoustic features of speech, such as the speech envelope and formant structure of the stimulus. The best indication of whether or not a hearing aid is providing benefit lies in the patient's speech perception using the device. The FFR, which provides neural correlates of speech perception, can provide an objective measure of the benefit from amplification (e.g. in terms of F0 encoding and formant encoding). Further, given that experience dependent effects can influence subcortical pitch encoding, the FFR may also serve as a tool to track "secondary plasticity" following amplification and auditory training through pre- and post-training/amplification recordings in HI listeners. Additionally, understanding the neural underpinnings of pitch encoding at the level of the brainstem in hearing impairment may aid in the development of new and improved signal processing strategies that can be implemented in amplification devices and auditory prostheses.

The results of this dissertation establish the FFR as a viable technique to measure brainstem speech encoding in HI listeners to a range of stimuli in a variety of listening conditions. Translation of the brainstem FFR from the lab to the clinic would add great value to the existing audiological test battery.

10.3 Concluding statement

The vagaries of SNHL render it a puzzle to researchers, audiologists and patients, even after several decades of research. Thus far, behavioral studies have dominated much of our knowledge regarding the effects of SNHL in humans, while neurophysiologic studies in animals have yielded information about the neural manifestations of hearing loss. The experiments conducted as part of this dissertation aim to bridge findings from perceptual studies in humans and experiments in animal models using an objective, non-invasive, neural index of brainstem pitch encoding, namely the FFR. By using the FFR, perceptual deficits seen in SNHL are mapped to underlying neural mechanisms that drive the auditory system, adding one more piece of information to the jigsaw puzzle that is hearing impairment.

LIST OF REFERENCES

LIST OF REFERENCES

Abrams, D., & Kraus, N. (2009). Auditory pathway representations of speech sounds in humans. *Issues in Hand Book of Clinical …*. Retrieved from http://www.soc.northwestern.edu/brainvolts/documents/Abrams_Kraus_2008_Katz_Chapter_FINAL_AllReviews.pdf

Aiken, S. J., & Picton, T. W. (2008a). Human cortical responses to the speech envelope. *Ear and hearing*, *29*(2), 139–57. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18595182

Aiken, S. J., & Picton, T. W. (2008b). Envelope and spectral frequency-following responses to vowel sounds. *Hearing research*, *245*(1-2), 35–47. doi:10.1016/j.heares.2008.08.004

Akhoun, I., Gallégo, S., Moulin, a, Ménard, M., Veuillet, E., Berger-Vachon, C., … Thai-Van, H. (2008). The temporal relationship between speech auditory brainstem responses and the acoustic pattern of the phoneme /ba/ in normal-hearing adults. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, *119*(4), 922–33. doi:10.1016/j.clinph.2007.12.010

Anderson, D.J., Rose, J.E., Hind, J.E., Brugge, J.F., 1971. Temporal position of discharges in single auditory nerve fibers within the cycle of a sine-wave stimulus: frequency and intensity effects. J. Acoust. Soc. Am. 49 (4, Suppl. 2), 1131–1139.

Anderson, S., & Kraus, N. (2010). Objective neural indices of speech-in-noise perception. *Trends in amplification*, *14*(2), 73–83. doi:10.1177/1084713810380227

Anderson, S., Parbery-Clark, A., White-Schwoch, T., Drehobl, S., & Kraus, N. (2013). Effects of hearing loss on the subcortical representation of speech cues. *The Journal of the Acoustical Society of America*, *133*(5), 3030–8. doi:10.1121/1.4799804

Anderson, S., Skoe, E., Chandrasekaran, B., & Kraus, N. (2010). Neural timing is linked to speech perception in noise. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *30*(14), 4922–6. doi:10.1523/JNEUROSCI.0107-10.2010

Anderson, S., Skoe, E., Chandrasekaran, B., Zecker, S., & Kraus, N. (2010). Brainstem correlates of speech-in-noise perception in children. *Hearing research*, *270*(1-2), 151–7. doi:10.1016/j.heares.2010.08.001

Ardoint, M., Sheft, S., Fleuriot, P., Garnier, S., & Lorenzi, C. (2010). Perception of temporal fine-structure cues in speech with minimal envelope cues for listeners with mild-to-moderate hearing loss. *International journal of audiology*,*49*(11), 823-831.

Arehart, K. H. (1994). Effects of harmonic content on complex-tone fundamental-frequency discrimination in hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *95*, 3574.

Assmann, P. F., & Summerfield, Q. (1987). Perceptual segregation of concurrent vowels. *The Journal of the Acoustical Society of America*, *82*, S120.

Assmann, P. F., & Summerfield, Q. (1989). Modeling the perception of concurrent vowels: Vowels with the same fundamental frequency. *The Journal of the Acoustical Society of America*, *85*, 327.

Assmann, P., & Summerfield, Q. (2004). The perception of speech under adverse conditions. In *Speech processing in the auditory system* (pp. 231-308). Springer New York.

Bacon, S. P., & Gleitman, R. M. (1992). Modulation detection in subjects with relatively flat hearing losses. *Journal of Speech, Language and Hearing Research*, *35*(3), 642.

Bacon, S., Opie, J., & Montoya, D. (1998). The effects of hearing loss and noise masking on the masking release for speech in temporally complex backgrounds. ... *of Speech, Language and Hearing* .... Retrieved from http://jslhr.asha.org/cgi/content/abstract/41/3/549

Bacon SP, Viemester NF (1985) Temporal modulation transfer function in normal hearing and hearing impaired subjects, Audiology 24:117-134

Banai, K., Hornickel, J., Skoe, E., Nicol, T., Zecker, S., & Kraus, N. (2009). Reading and Subcortical Auditory Function, (November), 2699–2707. doi:10.1093/cercor/bhp024

Banai, K., Nicol, T., Zecker, S. G., & Kraus, N. (2005). Brainstem timing: implications for cortical processing and literacy. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *25*(43), 9850–7. doi:10.1523/JNEUROSCI.2373-05.2005

Baer, T., Moore, B. C., & Gatehouse, S. (1993). Spectral contrast enhancement of speech in noise for listeners with sensorineural hearing impairment: effects on intelligibility, quality, and response times. *Journal of rehabilitation research and development*, *30*, 49-49.

Başkent, D. (2006). Speech recognition in normal hearing and sensorineural hearing loss as a function of the number of spectral channels. *The Journal of the Acoustical Society of America*, *120*(5), 2908. doi:10.1121/1.2354017

Berglund, B., Hassmén, P., & Job, R. F. (1996). Sources and effects of low-frequency noise. *The Journal of the Acoustical Society of America*, *99*(5), 2985–3002. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21768734

Bidelman, G., & Krishnan, A. (2010). Effects of reverberation on brainstem representation of speech in musicians and non-musicians. *Brain research*, 112–125. doi:10.1016/j.brainres.2010.07.100.Effects

Bidelman, G. M., Gandour, J. T., & Krishnan, A. (2011). Cross-domain effects of music and language experience on the representation of pitch in the human auditory brainstem. *Journal of cognitive neuroscience*, *23*(2), 425–34. doi:10.1162/jocn.2009.21362

Boatman, D. F. (2006). Cortical auditory systems: speech and other complex sounds. *Epilepsy & behavior : E&B*, *8*(3), 494–503. doi:10.1016/j.yebeh.2005.12.012

Boettcher, F. a, Poth, E. a, Mills, J. H., & Dubno, J. R. (2001). The amplitude-modulation following response in young and aged human subjects. *Hearing research*, *153*(1-2), 32–42. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11223295

Boettcher, F. A., Madhotra, D., Poth, E. A., & Mills, J. H. (2002). The frequency-modulation following response in young and aged human subjects. *Hearing research*, *165*(1), 10-18.

Brugge, J. F., Anderson, D. J., Hind, J. E., & Rose, J. E. (1969). Time structure of discharges in single auditory nerve fibers of the squirrel monkey in response to complex periodic sounds. *Journal of Neurophysiology*.

Buss, E., Hall, J. W., & Grose, J. H. (2004). Temporal Fine-Structure Cues to Speech and Pure Tone Modulation in Observers with Sensorineural Hearing Loss. *Ear and Hearing*, *25*(3), 242–250. doi:10.1097/01.AUD.0000130796.73809.09

Buus, S., & Florentine, M. (1985). Gap detection in normal and impaired listeners: The effect of level and frequency. In *Time resolution in auditory systems* (pp. 159-179). Springer Berlin Heidelberg.

Carney LH, Heinz MG, Evilsizer ME, Gilkey RH, Colburn HS. Auditory phase opponency: A temporal model for masked detection at low frequencies. Acta Acust. Acust. 88:334–346, 2002.

Cariani, P. a, & Delgutte, B. (1996a). Neural correlates of the pitch of complex tones. II. Pitch shift, pitch ambiguity, phase invariance, pitch circularity, rate pitch, and the dominance region for pitch. *Journal of neurophysiology*, *76*(3), 1717–34. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8890287

Cariani, P., & Delgutte, B. (1996b). Neural correlates of the pitch of complex tones. I. Pitch and pitch salience. *Journal of Neurophysiology*. Retrieved from http://jn.physiology.org/content/76/3/1698.short

Chambers, R., Feth, L., & Burns, E. (1986). The relation between the human frequency-following response and the low pitch of complex tones. *The Journal of the Acoustical Society ...*, 1673–1680. Retrieved from http://link.aip.org/link/?JASMAN/80/1673/1

Chandrasekaran, B, & Kraus, N. (2010). The scalp-recorded brainstem response to speech: Neural origins and plasticity. *Psychophysiology*, *47*(2), 236–246. doi:10.1111/j.1469-8986.2009.00928.x.The

Chandrasekaran, Bharath, Hornickel, J., Skoe, E., Nicol, T., & Kraus, N. (2009). Context-dependent encoding in the human auditory brainstem relates to hearing speech in noise: implications for developmental dyslexia. *Neuron*, *64*(3), 311–9. doi:10.1016/j.neuron.2009.10.006

Chandrasekaran, Bharath, & Kraus, N. (2010). The scalp-recorded brainstem response to speech: neural origins and plasticity. *Psychophysiology*, *47*(2), 236–46. doi:10.1111/j.1469-8986.2009.00928.x

Ching, T. Y., Dillon, H., & Byrne, D. (1998). Speech recognition of hearing-impaired listeners: predictions from audibility and the limited role of high-frequency amplification. *The Journal of the Acoustical Society of America*, *103*(2), 1128–40. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9479766

Clinard, C. G., Tremblay, K. L., & Krishnan, A. R. (2010). Aging alters the perception and physiological representation of frequency: evidence from human frequency-following response recordings. *Hearing research*, *264*(1-2), 48–55. doi:10.1016/j.heares.2009.11.010

Cunningham, J., Nicol, T., & Zecker, S. (2001). Neurobiologic responses to speech in noise in children with learning problems: deficits and strategies for improvement. *Clinical ...*, *112*, 758–767. Retrieved from http://www.sciencedirect.com/science/article/pii/S1388245701004655

Daly, D., Roeser, R., & Moushegian, G. (1976). The frequency-following response in subjects with profound unilateral hearing loss. *Electroencephalography and clinical neurophysiology*, *40(2), 132-142*. Retrieved from http://www.sciencedirect.com/science/article/pii/0013469476901589

Davis, H., & Hirsh, S. K. (1976). The Audiometric Utility of Brains Stem Responses to Low-Frequency Sounds. *Audiology*, 181–195.

Desloge, J. G., Reed, C. M., Braida, L. D., Perez, Z. D., & Delhorne, L. a. (2011a). Temporal modulation transfer functions for listeners with real and simulated hearing loss. *The Journal of the Acoustical Society of America*, *129*(6), 3884–96. doi:10.1121/1.3583550

Desloge, J. G., Reed, C. M., Braida, L. D., Perez, Z. D., & Delhorne, L. a. (2011b). Temporal modulation transfer functions for listeners with real and simulated hearing loss. *The Journal of the Acoustical Society of America*, *129*(6), 3884–96. doi:10.1121/1.3583550

Dietrich, V., Nieschalk, M., Stoll, W., Rajan, R., & Pantev, C. (2001). Cortical reorganization in patients with high frequency cochlear hearing loss. *Hearing research*, *158*(1-2), 95–101. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11506941

Dirks, D. D., Morgan, D. E., & Dubno, J. R. (1982). A procedure for quantifying the effects of noise on speech recognition. *Journal of Speech and Hearing Disorders*, *47*(2), 114.

Dorman, M. F., Marton, K., Hannley, M. T., & Lindholm, J. M. (1985). Phonetic identification by elderly normal and hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *77*, 664.

Dreschler, W. A., & Plomp, R. (1980). Relation between psychophysical data and speech perception for hearing-impaired subjects. I. *The Journal of the Acoustical Society of America*, *68*, 1608.

Drullman, R., Festen, J. M., & Plomp, R. (1994). Effect of temporal envelope smearing on speech reception. *The Journal of the Acoustical Society of America*, *95*(2), 1053–64. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8132899

Dubno, J. R., & Dirks, D. D. (1990). Associations among frequency and temporal resolution and consonant recognition for hearing-impaired listeners.*Acta oto-laryngologica*. *Supplementum*, *469*, 23.

Dubno, J. R., & Dirks, D. D. (1989). Auditory filter characteristics and consonant recognition for hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *85*, 1666.

Dubno, J., & Schaefer, A. (1992). Comparison of frequency selectivity and consonant recognition among hearing-impaired and masked normal-hearing listeners. *The Journal of the Acoustical Society of …*. Retrieved from http://link.aip.org/link/?JASMAN/91/2110/1

Dubno, J. R., & Schaefer, A. B. (1995). Frequency selectivity and consonant recognition for hearing-impaired and normal-hearing listeners with equivalent masked thresholds. *The Journal of the Acoustical Society of America*, *97*(2), 1165-1174.

Duquesnoy, a J., & Plomp, R. (1980). Effect of reverberation and noise on the intelligibility of sentences in cases of presbyacusis. *The Journal of the Acoustical Society of America*, *68*(2), 537–44. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7419810

Duquesnoy, a J., & Plomp, R. (1983). The effect of a hearing aid on the speech-reception threshold of hearing-impaired listeners in quiet and in noise. *The Journal of the Acoustical Society of America*, *73*(6), 2166–73. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/6875102

Edwards, B. (2004). Hearing aids and hearing impairment. In *Speech processing in the auditory system* (pp. 339-421). Springer New York.

Festen, J. M., & Plomp, R. (1990). Effects of fluctuating noise and interfering speech on the speech-reception threshold for impaired and normal hearing. *The Journal of the Acoustical Society of America*, *88*(4), 1725–36. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2262629

Fitzgibbons, P. J., & Gordon-Salant, S. (1987). Minimum stimulus levels for temporal gap resolution in listeners with sensorineural hearing loss. *The Journal of the Acoustical Society of America*, *81*, 1542.

Fitzgibbons, P. J., & Gordon-Salant, S. (1987). Temporal gap resolution in listeners with high-frequency sensorineural hearing loss. *The Journal of the Acoustical Society of America*, *81*, 133.

Fitzgibbons, P., & Wightman, F. (1982). Gap detection in normal and hearing-impaired listeners. *The Journal of the Acoustical Society of …*, *72*(3), 761–765. Retrieved from http://link.aip.org/link/?JASMAN/72/761/1

Florentine, M., & Buus, S. (1984). Temporal gap detection in sensorineural and simulated hearing impairments. *Journal of Speech, Language and Hearing Research*, *27*(3), 449.

Florentine, M., Fastl, H., & Buus, S. (1988). Temporal integration in normal hearing, cochlear impairment, and impairment simulated by masking. *The Journal of the Acoustical Society of America*, *84*, 195.

Florentine, M., Reed, C. M., Rabinowitz, W. M., Braida, L. D., Durlach, N. I., & Buus, S. (1993). Intensity perception. XIV. Intensity discrimination in listeners with sensorineural hearing loss. *The Journal of the Acoustical Society of America*, *94*, 2575.

Fodor, J. (1983). *The Modularity of mind [electronic resource]: an essay on faculty psychology*. The MIT Press.

Festen, J. M., & Plomp, R. (1983). Relations between auditory functions in impaired hearing. *The Journal of the Acoustical Society of America*, *73*, 652.

Freyman, R., & Nelson, D. (1986). Frequency discrimination as a function of tonal duration and excitation-pattern slopes in normal and hearing-impaired listeners. *The Journal of the Acoustical Society of* …. Retrieved from http://link.aip.org/link/?jasman/79/1034/1

Freyman, R. L., & Nelson, D. A. (1991). Frequency discrimination as a function of signal frequency and level in normal-hearing and hearing-impaired listeners.*Journal of Speech, Language and Hearing Research*, *34*(6), 1371.

Frisina, D. R., & Frisina, R. D. (1997). Speech recognition in noise and presbycusis: relations to possible neural mechanisms. *Hearing Research*, *106*(1-2), 95–104. doi:10.1016/S0378-5955(97)00006-3

Füllgrabe, C., Meyer, B., & Lorenzi, C. (2003). Effect of cochlear damage on the detection of complex temporal envelopes. *Hearing research*, *178*(1), 35-43.

Gagné, J. P. (1988). Excess masking among listeners with a sensorineural hearing loss. *The Journal of the Acoustical Society of America*, *83*(6), 2311–21. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3411023

Galbraith, G. C., Threadgill, M. R., Hemsley, J., Salour, K., Songdej, N., Ton, J., & Cheung, L. (2000). Putative measure of peripheral and brainstem frequency-following in humans. *Neuroscience Letters*, (292), 123–127.

Galbraith, G. C. (1994). Two-channel brain-stem frequency-following responses to pure tone and missing fundamental stimuli. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *92*(4), 321-330.

Gardi, J., & Merzenich, M. (1979). The effect of high-pass noise on the scalp-recorded frequency following response (FFR) in humans and cats. *The Journal of the Acoustical Society of America*, *65*(June 1979), 1491–1500. Retrieved from http://link.aip.org/link/?JASMAN/65/1491/1

Gardi, J., Merzenich, M., & McKean, C. (1979). Origins of the scalp-recorded frequency-following response in the cat. *International Journal of Audiology*,*18*(5), 353-380.

Gengel, R. W. (1973). Temporal effects in frequency discrimination by hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *54*(1), 11–5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/4731641

George, E. L., Goverts, S. T., Festen, J. M., & Houtgast, T. (2010). Measuring the effects of reverberation and noise on sentence intelligibility for hearing-impaired listeners. *Journal of Speech, Language and Hearing Research*, *53*(6), 1429. Retrieved from http://jslhr.asha.org/cgi/content/abstract/53/6/1429

Gerken, G. M., Moushegian, G., Stillman, R. D., & Rupert, A. L. (1975). Human Frequency-Following Responses to Monaural and Binaural Stimuli. *Electroencephalography and Clinical Neurophysiology*, *38*, 379–386.

Glasberg, B. R., & Moore, B. C. (1986). Auditory filter shapes in subjects with unilateral and bilateral cochlear impairments. *The Journal of the Acoustical Society of America*, *79*, 1020.

Glasberg, B. R., & Moore, B. C. (1992). Effects of envelope fluctuations on gap detection. *Hearing research*, *64*(1), 81–92. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1490904

Glaser, E. M., Suter, C. M., Dasheiff, R., & Goldberg, a. (1976). The human frequency-following response: its behavior during continuous tone and tone burst stimulation. *Electroencephalography and clinical neurophysiology*, *40*(1), 25–32. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/55345

Goldstein, J., & Srulovicz, P. (1977). Auditory-nerve spike intervals as an adequate basis for aural frequency measurement. *Psychophysics and physiology of hearing*. Retrieved from http://www.kth.se/en/ees/forskning/2.8001/2.8276/courses/FEN3100/docs/Goldstein1977.pdf

Gootjes L, Raij T, Salmelin R, Hari R (1999): Left-hemisphere dominance for processing of vowels: a whole-scalp neuromagnetic study. Neuroreport 10:2987–2991.

Gordon-Salant, S. (2005). Hearing loss and aging: New research findings and clinical implications. *The Journal of Rehabilitation Research and Development*, *42*(4s), 9. doi:10.1682/JRRD.2005.01.0006

Gordon-Salant, S., Yeni-Komshian, G. H., Fitzgibbons, P. J., & Barrett, J. (2006). Age-related differences in identification and discrimination of temporal cues in speech segments. *The Journal of the Acoustical Society of America*, *119*(4), 2455. doi:10.1121/1.2171527

Greenberg, S, Marsh, J. T., Brown, W. S., & Smith, J. C. (1987). Neural temporal coding of low pitch. I. Human frequency-following responses to complex tones. *Hearing Research*, *25*(2-3), 91–114. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3558136

Greenberg, S., Smith, J. C., Marsh, J. T., & Brown, W. S. (1978). Human frequency following response to synthetic vowels. *The Journal of the Acoustical Society of America*, *63*, S76. Retrieved from http://link.aip.org/link/?JASMAN/63/S76/1

Greenberg, Steven, Marsh, J. T., Brown, W. S., & Smith, J. C. (1987). Neural temporal coding of low pitch. I. Human frequency-following responses to complex tones. *Hearing research*, 91–114.

Grose, J. H., Mamo, S. K., & Hall, J. W. (2009). Age effects in temporal envelope processing: speech unmasking and auditory steady state responses. *Ear and hearing*, *30*(5), 568–75. doi:10.1097/AUD.0b013e3181ac128f

Hall, J. (1979). Auditory brainstem frequency following responses to waveform envelope periodicity. *Science*, *205*(4412), 1297–1299. Retrieved from http://www.sciencemag.org/content/205/4412/1297.short

Hall, J. W., & Wood, E. J. (1984). Stimulus duration and frequency discrimination for normal-hearing and hearing-impaired subjects. *Journal of Speech, Language and Hearing Research*, *27*(2), 252.

Harrison, R., & Evans, E. (1979). Some aspects of temporal coding by single cochlear fibres from regions of cochlear hair cell degeneration in the guinea pig. *Archives of oto-rhino-laryngology*. Retrieved from http://link.springer.com/article/10.1007/BF00455226

He, N., Mills, J. H., Ahlstrom, J. B., & Dubno, J. R. (2008). Age-related differences in the temporal modulation transfer function with pure-tone carriers. *The Journal of the Acoustical Society of America*, *124*(6), 3841–9. doi:10.1121/1.2998779

Heinz, M G, Colburn, H. S., & Carney, L. H. (2001). Evaluating auditory performance limits: i. one-parameter discrimination using a computational model for the auditory nerve. *Neural computation*, *13*(10), 2273–316. doi:10.1162/089976601750541804

Heinz, M. (2012). Physiological Correlates of Perceptual Deficits Following Sensorineural Hearing Loss. *Acoustics Today*, *8*(2). Retrieved from http://link.aip.org/link/?ATCODK/8/34/1

Heinz, Michael G, & Swaminathan, J. (2009). Quantifying envelope and fine-structure coding in auditory nerve responses to chimaeric speech. *Journal of the Association for Research in Otolaryngology : JARO*, *10*(3), 407–23. doi:10.1007/s10162-009-0169-8

Heinz, Michael G, & Young, E. D. (2004). Response growth with sound level in auditory-nerve fibers after noise-induced hearing loss. *Journal of neurophysiology*, *91*(2), 784–95. doi:10.1152/jn.00776.2003

Henry, J. (2013). *Pitch Neural Coding and Perception*. *International journal of audiology*. Retrieved from http://informahealthcare.com/doi/pdf/10.3109/14992027.2012.754109

Henry, K. S., & Heinz, M. G. (2012). Diminished temporal coding with sensorineural hearing loss emerges in background noise. *Nature neuroscience*, *15*(10), 1362–4. doi:10.1038/nn.3216

Henry, K. S., & Heinz, M. G. (2013a). Effects of sensorineural hearing loss on temporal coding of narrowband and broadband signals in the auditory periphery. *Hearing research*, 1–9. doi:10.1016/j.heares.2013.01.014

Henry, K. S., & Heinz, M. G. (2013b). Effects of sensorineural hearing loss on temporal coding of narrowband and broadband signals in the auditory periphery. *Hearing research*, *303*, 39–47. doi:10.1016/j.heares.2013.01.014

Henry, K. S., Kale, S., Scheidt, R. E., & Heinz, M. G. (2011). Auditory brainstem responses predict auditory nerve fiber thresholds and frequency selectivity in hearing impaired chinchillas. *Hearing research*, *280*(1-2), 236–44. doi:10.1016/j.heares.2011.06.002

Hogan, C. A., & Turner, C. W. (1998). High-frequency audibility: Benefits for hearing-impaired listeners. *The Journal of the Acoustical Society of America*,*104*, 432.

Hoormann, J., Falkenstein, M., Hohnsbein, J., & Blanke, L. (1992). The human-frequency following response (FFR): Normal variability and relation to the click evoked brainstem response. *Hearing research*, (59), 179–188.

Hopkins, K., & Moore, B. C. (2007). Moderate cochlear hearing loss leads to a reduced ability to use temporal fine structure information. *The Journal of the Acoustical Society of America*, *122*, 1055.

Hopkins, K., & Moore, B. C. J. (2011). The effects of age and cochlear hearing loss on temporal fine structure sensitivity, frequency selectivity, and speech reception in noise. *The Journal of the Acoustical Society of America*, *130*(1), 334–49. doi:10.1121/1.3585848

Hopkins, K., Moore, B., & Stone, M. (2008). Effects of moderate cochlear hearing loss on the ability to benefit from temporal fine structure information in speech. *The Journal of the Acoustical Society …*, *123*(2), 1140–1153. doi:10.1121/1.2824018.Effects

Horwitz, A. R., Dubno, J. R., & Ahlstrom, J. B. (2002). Recognition of low-pass-filtered consonants in noise with normal and impaired high-frequency hearing.*The Journal of the Acoustical Society of America*, *111*, 409.

Huss M, Moore BCJ. Dead regions and pitch perception. J. Acoust. Soc. Am. 117:3841–3852, 2005

Hall, J. H., Buss, E., & Grose, J. (2008). The effect of hearing impairment on the identification of speech that is modulated synchronously or asynchronously across frequency. *The Journal of the Acoustical Society of …*, (February), 955–962. doi:10.1121/1.2821967

Jesteadt, W., Bilger, R. C., Green, D. M., & Patterson, J. H. (1976). Temporal acuity in listeners with sensorineural hearing loss. *Journal of Speech, Language and Hearing Research*, *19*(2), 357.

Johnson, D. H. (1980). The relationship between spike rate and synchrony in responses of auditory-nerve fibers to single tones. *The Journal of the Acoustical Society of America*, *68*, 1115.

Johnson, K. L., Nicol, T., Zecker, S. G., & Kraus, N. (2008). Developmental plasticity in the human auditory brainstem. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *28*(15), 4000–7. doi:10.1523/JNEUROSCI.0012-08.2008

Joris, P., & Yin, T. (1992). Responses to amplitude-modulated tones in the auditory nerve of the cat. *The Journal of the Acoustical Society of America*. Retrieved from http://link.aip.org/link/?JASMAN/91/215/1

Jr, T. G., & Pfeiffer, R. (1968). A Test for Cochlear Linearity from Cochlear Nerve Spike Discharges in Response to Combination Click Stimuli. *The Journal of the Acoustical Society of ...*, 2013. Retrieved from http://link.aip.org/link/?JASMAN/44/363/5

Kale, S., & Heinz, M. G. (2010). Envelope coding in auditory nerve fibers following noise-induced hearing loss. *Journal of the Association for Research in Otolaryngology*, *11*(4), 657-673.

Kewley-Port, D. (1982). Measurement of formant transitions in naturally produced stop consonant–vowel syllables. *The Journal of the Acoustical Society of America*, *72*, 379.

King, C., Warrier, C. M., Hayes, E., & Kraus, N. (2002). Deficits in auditory brainstem pathway encoding of speech sounds in children with learning problems. *Neuroscience letters*, *319*(2), 111–5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11825683

Korczak, P., Kurtzberg, D., & Stapells, D. (2005). Effects of sensorineural hearing loss and personal hearing aids on cortical event-related potential and behavioral measures of speech-sound processing. *Ear and hearing*, (410). Retrieved from http://journals.lww.com/ear-hearing/Abstract/2005/04000/Effects_of_Sensorineural_Hearing_Loss_and_Personal.5.aspx

Kraus, N., & Nicol, T. (2005). Brainstem origins for cortical 'what'and 'where'pathways in the auditory system. *Trends in neurosciences*, *28*(4), 176-181.

Krishnan, A. (1999). Human frequency-following responses to two-tone approximations of steady-state vowels. *Audiology and Neurotology*, *4*(2), 95-103.

Krishnan, A, Gandour, J., & Bidelman, G. (2012). Experience-dependent plasticity in pitch encoding: from brainstem to auditory cortex. *Neuroreport*, *23*(8), 498–502. doi:10.1097/WNR.0b013e328353764d.Experience-dependent

Krishnan, Ananthanarayan. (2002a). Human frequency-following responses: representation of steady-state synthetic vowels. *Hearing research*, *166*(1-2), 192–201. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12062771

Krishnan, Ananthanarayan. (2002b). Human frequency-following responses: representation of steady-state synthetic vowels. *Hearing research*, *166*(1-2), 192–201. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12062771

Krishnan, Ananthanarayan, Gandour, J. T., Smalt, C. J., & Gavin, M. (2011). is not limited to acceleration rates that occur in natural speech, *114*(3), 193–198. doi:10.1016/j.bandl.2010.05.004.Language-dependent

Krishnan, A., & Parkinson, J. (2000). Human frequency-following response: representation of tonal sweeps. *Audiology and Neurotology*, *5*(6), 312-321.

Krishnan, Ananthanarayan, Swaminathan, J., & Gandour, J. T. (2009). Experience-dependent enhancement of linguistic pitch representation in the brainstem is not specific to a speech context. *Journal of cognitive neuroscience*, *21*(6), 1092–105. doi:10.1162/jocn.2009.21077

Krishnan, Ananthanarayan, Xu, Y., Gandour, J., & Cariani, P. (2005). Encoding of pitch in the human brainstem is sensitive to language experience. *Brain research. Cognitive brain research*, *25*(1), 161–8. doi:10.1016/j.cogbrainres.2005.05.004

Krishnan, Ananthanarayan, Xu, Y., Gandour, J. T., & Cariani, P. a. (2004). Human frequency-following response: representation of pitch contours in Chinese tones. *Hearing research*, *189*(1-2), 1–12. doi:10.1016/S0378-5955(03)00402-7

Kuwada, S., Batra, R., & Maher, V. (1986). Scalp potentials of normal and hearing-impaired subjects in response to sinusoidally amplitude-modulated tones. *Hearing research*. Retrieved from http://www.sciencedirect.com/science/article/pii/0378595586900389

Lataye, R., & Campo, P. (1997). Combined effects of a simultaneous exposure to noise and toluene on hearing function. *Neurotoxicology and teratology*, *19*(5), 373–82. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9380004

Leek, M. R., & Molis, M. R. Beyond Audibility.

Leek, M. R., & Summers, V. (1996). Reduced frequency selectivity and the preservation of spectral, (April), 1796–1806.

Leek, M., & Summers, V. (1996). Reduced frequency selectivity and the preservation of spectral contrast in noise. *The Journal of the Acoustical Society of America*, (April), 1796–1806. Retrieved from http://link.aip.org/link/?JASMAN/100/1796/1

Li, X., & Jeng, F.-C. (2011). Noise tolerance in human frequency-following responses to voice pitch. *The Journal of the Acoustical Society of America*, *129*(1), EL21–6. doi:10.1121/1.3528775

Liberman, A. M., Delattre, P. C., Cooper, F. S., & Gerstman, L. J. (1954). The role of consonant-vowel transitions in the perception of the stop and nasal consonants. *Psychological Monographs: General and Applied*, *68*(8), 1.

Liberman, a M., & Mattingly, I. G. (1985). The motor theory of speech perception revised. *Cognition*, *21*(1), 1–36. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/4075760

Liberman, A. M., Liberman, I., Mann, V., Manuel, S., Mattingly, I., Repp, B., & I, M. S. (1981). ON FINDING THAT SPEECH IS SPECIAL* Alvin M. Liberman+, *68*, 107–144.

Loeb GE, White MW, Merzenich MM. Spatial cross correlation: A proposed mechanism for acoustic pitch perception. Biol. Cybern. 47:149–163, 1983.[PubMed]

Lorenzi, C., Debruille, L., Garnier, S., Fleuriot, P., & Moore, B. C. J. (2009). Abnormal processing of temporal fine structure in speech for frequencies where absolute thresholds are normal. *The Journal of the Acoustical Society of America*, *125*(1), 27–30. doi:10.1121/1.2939125

Lorenzi, C., Gilbert, G., Carn, H., Garnier, S., & Moore, B. C. J. (2006). Speech perception problems of the hearing impaired reflect inability to use temporal fine structure. *Proceedings of the National Academy of Sciences of the United States of America*, *103*(49), 18866–9. doi:10.1073/pnas.0607364103

Marsh, J. T., Brown, W. S., & Smith, J. C. (1974). Differential brainstem pathways for the conduction of auditory frequency-following responses.*Electroencephalography and clinical neurophysiology*, *36*, 415-424. Retrieved from http://www.sciencedirect.com/science/article/pii/0013469474901928

Marsh, J. T., Brown, W. S., & Smith, J. C. (1975). Far-field recorded frequency-following responses: Correlates of low pitch auditory perception in humans Responses d'entertainement enregistrees a distance: Correlates de la perception auditive des sons de faible hauteur chez l'homme.*Electroencephalography and clinical neurophysiology*, *38*(2), 113-119.

Marsh, J., Worden, F., & Smith, J. (1970). Auditory frequency-following response: neural or artifact? *Science*, *169*(3951), 1222–1223. Retrieved from http://www.sciencemag.org/content/169/3951/1222.short

Meddis, R., & O'Mard, L. (1997). A unitary model of pitch perception. *The Journal of the Acoustical Society of America*, *102*(3), 1811–20. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9714929

Miller, R. L., Schilling, J. R., Franck, K. R., & Young, E. D. (1997). Effects of acoustic trauma on the representation of the vowel "eh" in cat auditory nerve fibers. *The Journal of the Acoustical Society of America*, *101*(6), 3602–16. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9193048

Molis, M. R., & Leek, M. R. (2012). NIH Public Access, *54*(4), 1211–1223. doi:10.1044/1092-4388(2010/09-0218).Vowel

Møller, A. R., Jannetta, P. J., & Sekhar, L. N. (1988). Contributions from the auditory nerve to the brain-stem auditory evoked potentials (BAEPs): results of intracranial recording in man. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *71*(3), 198-211.

Moore, B. (1996). Perceptual consequences of cochlear hearing loss and their implications for the design of hearing aids. *Ear and hearing*, *17*(April 1996), 133–161. Retrieved from http://journals.lww.com/ear-hearing/Abstract/1996/04000/Perceptual_Consequences_of_Cochlear_Hearing_Loss.7.aspx

Moore, B. C. J. (2002). Interference effects and phase sensitivity in hearing. *Philosophical transactions. Series A, Mathematical, physical, and engineering sciences*, *360*(1794), 833–58. doi:10.1098/rsta.2001.0970

Moore, B. C. J. (2008). The role of temporal fine structure processing in pitch perception, masking, and speech perception for normal-hearing and hearing-impaired people. *Journal of the Association for Research in Otolaryngology : JARO*, *9*(4), 399–406. doi:10.1007/s10162-008-0143-x

Moore, B. C., & Carlyon, R. P. (2005). Perception of pitch by people with cochlear hearing loss and by cochlear implant users. In *Pitch* (pp. 234-277). Springer New York.

Moore, B. C., & Moore, B. C. (2003). *An introduction to the psychology of hearing* (Vol. 4). San Diego: Academic press.

Moore, B. C., & Glasberg, B. R. (1993). Simulation of the effects of loudness recruitment and threshold elevation on the intelligibility of speech in quiet and in a background of speech. *The Journal of the Acoustical Society of America*, *94*, 2050.

Moore, B. C., & Glasberg, B. R. (1988). Gap detection with sinusoids and noise in normal, impaired, and electrically stimulated ears. *The Journal of the Acoustical Society of America*, *83*, 1093.

Moore, B. C., Glasberg, B. R., Donaldson, E., McPherson, T., & Plack, C. J. (1989). Detection of temporal gaps in sinusoids by normally hearing and hearing-impaired subjects. *The Journal of the Acoustical Society of America*,*85*, 1266.

Moore, B. C. J., Glasberg, B. R., & Hopkins, K. (2006). Frequency discrimination of complex tones by hearing-impaired subjects: Evidence for loss of ability to use temporal fine structure. *Hearing research*, *222*(1-2), 16–27. doi:10.1016/j.heares.2006.08.007

Moore, B. C., Peters, R. W., & Glasberg, B. R. (1992). Detection of temporal gaps in sinusoids by elderly subjects with and without hearing loss. *The Journal of the Acoustical Society of America*, *92*(4 Pt 1), 1923–32.

Moore, B. C., & Glasberg, B. R. (1988). Gap detection with sinusoids and noise in normal, impaired, and electrically stimulated ears. *The Journal of the Acoustical Society of America*, *83*, 1093. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3356814

Moushegian, G., Rupert, a L., & Stillman, R. D. (1973). Laboratory note. Scalp-recorded early responses in man to frequencies in the speech range. *Electroencephalography and clinical neurophysiology*, *35*(6), 665–7. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/4128165

Musacchia, G., Sams, M., Skoe, E., & Kraus, N. (2007). Musicians have enhanced subcortical auditory and audiovisual processing of speech and music. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(40), 15894–8. doi:10.1073/pnas.0701498104

Nábělek, a K. (1988). Identification of vowels in quiet, noise, and reverberation: relationships with age and hearing loss. *The Journal of the Acoustical Society of America*, *84*(2), 476–84. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3170940

Nábělek, a K., & Dagenais, P. a. (1986). Vowel errors in noise and in reverberation by hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *80*(3), 741–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3760327

Nábělek, a K., Ovchinnikov, a, Czyzewski, Z., & Crowley, H. J. (1996). Cues for perception of synthetic and natural diphthongs in either noise or reverberation. *The Journal of the Acoustical Society of America*, *99*(3), 1742–53. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8819863

Nábělek, a K., & Robinson, P. K. (1982). Monaural and binaural speech perception in reverberation for listeners of various ages. *The Journal of the Acoustical Society of America*, *71*(5), 1242–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7085996

Nábělek, A. K., Letowski, T. R., & Tucker, F. M. (1989). Reverberant overlap-and self-masking in consonant identification. *The Journal of the Acoustical Society of America*, *86*, 1259. Retrieved from http://link.aip.org/link/?JASMAN/86/1259/1

Nelson, D. A., & Freyman, R. L. (1987). Temporal resolution in sensorineural hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *81*, 709.

Oates, P., Kurtzberg, D., & Stapells, D. R. (2002). Effects of sensorineural hearing loss on cortical event-related potential and behavioral measures of speech-sound processing. *Ear and hearing*, *23*(5), 399–415. doi:10.1097/01.AUD.0000034777.12562.31

Oxenham AJ, Bernstein JG, Penagos H. Correct tonotopic representation is necessary for complex pitch perception. Proc. Natl. Acad. Sci. U.S.A. 101:1421–1425, 2004. [PMC free article][PubMed]

Parbery-Clark, A., Skoe, E., & Kraus, N. (2009). Musical experience limits the degradative effects of background noise on the neural processing of sound. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *29*(45), 14100–7. doi:10.1523/JNEUROSCI.3256-09.2009

Parthasarathy, a, & Bartlett, E. L. (2011). Age-related auditory deficits in temporal processing in F-344 rats. *Neuroscience*, *192*, 619–30. doi:10.1016/j.neuroscience.2011.06.042

Parviainen, T., Helenius, P., & Salmelin, R. (2005a). Cortical differentiation of speech and nonspeech sounds at 100 ms: implications for dyslexia. *Cerebral cortex (New York, N.Y. : 1991)*, *15*(7), 1054–63. doi:10.1093/cercor/bhh206

Parviainen, T., Helenius, P., & Salmelin, R. (2005b). Cortical differentiation of speech and nonspeech sounds at 100 ms: implications for dyslexia. *Cerebral cortex (New York, N.Y. : 1991)*, *15*(7), 1054–63. doi:10.1093/cercor/bhh206

Pavlovic, C. V., Studebaker, G. A., & Sherbecoe, R. L. (1986). An articulation index based procedure for predicting the speech recognition performance of hearing-impaired individuals. *The Journal of the Acoustical Society of America*,*80*, 50.

Peters, R. W., & Moore, B. C. (1992). Auditory filter shapes at low center frequencies in young and elderly hearing-impaired subjects. *The Journal of the Acoustical Society of America*, *91*, 256.

Pichora-Fuller, M. K., & Singh, G. (2006). Effects of Age on Auditory and Cognitive Processing: Implications for Hearing Aid Fitting and Audiologic Rehabilitation. *Trends in Amplification*, *10*(1), 29–59. doi:10.1177/108471380601000103

Plomp, R. (1978). Auditory handicap of hearing impairment and the limited benefit of hearing aids. *The Journal of the Acoustical Society of America*, *63*, 533.

Plomp, R., & Mimpen, A. M. (1979). Speech-reception threshold for sentences as a function of age and noise level. *The Journal of the Acoustical Society of America*, *66*, 1333.

Plomp, R., & Duquesnoy, a J. (1980). Room acoustics for the aged. *The Journal of the Acoustical Society of America*, *68*(6), 1616–21. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7462459

Plomp, R., & Duquesnoy, A. J. (1982). A model for the speech-reception threshold in noise without and with a hearing aid. *Scandinavian audiology*. *Supplementum*, *15*, 95.

Plyler, P. N., & Ananthanarayan, a K. (2001). Human frequency-following responses: representation of second formant transitions in normal-hearing and hearing-impaired listeners. *Journal of the American Academy of Audiology*, *12*(10), 523–33. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11791939

Ponton, C. W., Don, M., Eggermont, J. J., Waring, M. D., Kwong, B., & Masuda, a. (1996). Auditory system plasticity in children after long periods of complete deafness. *Neuroreport*, *8*(1), 61–5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9051753

Price, C., Thierry, G., & Griffiths, T. (2005). Speech-specific auditory processing: where is it? *Trends in cognitive sciences*, *9*(6), 271–6. doi:10.1016/j.tics.2005.03.009

Purcell, D. W., John, S. M., Schneider, B. a., & Picton, T. W. (2004). Human temporal auditory acuity as assessed by envelope following responses. *The Journal of the Acoustical Society of America*, *116*(6), 3581. doi:10.1121/1.1798354

Qin, M. K., & Oxenham, A. J. (2005). Effects of envelope-vocoder processing on F0 discrimination and concurrent-vowel identification. *Ear and hearing*, *26*(5), 451–60. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16230895

Recio-Spinoso, A., Temchin, A. N., van Dijk, P., Fan, Y. H., & Ruggero, M. A. (2005). Wiener-kernel analysis of responses to noise of chinchilla auditory-nerve fibers. *Journal of neurophysiology*, *93*(6), 3615-3634.

Russo, N., Nicol, T., Trommer, B., Zecker, S., & Kraus, N. (2009). Brainstem transcription of speech is disrupted in children with autism spectrum disorders.*Developmental science*, *12*(4), 557-567. doi:10.1111/j.1467-7687.2008.00790.x.Brainstem

Russo, N. M., Nicol, T. G., Zecker, S. G., Hayes, E. a, & Kraus, N. (2005). Auditory training improves neural timing in the human brainstem. *Behavioural brain research*, *156*(1), 95–103. doi:10.1016/j.bbr.2004.05.012

Russo, Nicole, Nicol, T., Musacchia, G., & Kraus, N. (2004). Brainstem responses to speech syllables. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, *115*(9), 2021–30. doi:10.1016/j.clinph.2004.04.003

Sachs, M. B., Bruce, I. C., Miller, R. L., & Young, E. D. (2002). Biological Basis of Hearing-Aid Design. *Annals of Biomedical Engineering*, *30*(2), 157–168. doi:10.1114/1.1458592

Sachs, M., & Young, E. (1979). Encoding of steady-state vowels in the auditory nerve: Representation in terms of discharge rate. *The Journal of the Acoustical Society of America*. Retrieved from http://link.aip.org/link/?JASMAN/66/470/1

Sayles, M., & Winter, I. M. (2008). Reverberation challenges the temporal representation of the pitch of complex sounds. *Neuron*, *58*(5), 789–801. doi:10.1016/j.neuron.2008.03.029

Scheffler, K., Bilecen, D., & Schmid, N. (1998). Auditory cortical responses in hearing subjects and unilateral deaf patients as detected by functional magnetic resonance imaging. ... *cortex*, 156–163. Retrieved from http://cercor.oxfordjournals.org/content/8/2/156.short

Scherg, M., & Von Cramon, D. (1985). A new interpretation of the generators of BAEP waves I–V: results of a spatio-temporal dipole model.*Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *62*(4), 290-299.

Schilling, J., Miller, R., Sachs, M., & Young, E. (1998). Frequency-shaped amplification changes the neural representation of speech with noise-induced hearing loss. *Hearing research*, *117*, 57–70. Retrieved from http://www.sciencedirect.com/science/article/pii/S0378595598000033

Sellick PM, Patuzzi R, Johnstone BM. Measurement of basilar membrane motion in the guinea pig using the Mössbauer technique. J. Acoust. Soc. Am. 72:131–141, 1982. F

Semal, C., Demany, L., Ueda, K., & Hallé, P. A. (1996). Speech versus nonspeech in pitch memory. *The Journal of the Acoustical Society of America*,*100*, 1132. Retrieved from http://link.aip.org/link/?JASMAN/100/1132/1

Shailer, M. J., & Moore, B. C. (1983). Gap detection as a function of frequency, bandwidth, and level. *The Journal of the Acoustical Society of America*, *74*, 467.

Shamma, S., & Lorenzi, C. (2013a). On the balance of envelope and temporal fine structure in the encoding of speech in the early auditory system. *The Journal of the Acoustical Society of America*, *133*(5), 2818–33. doi:10.1121/1.4795783

Shamma, S., & Lorenzi, C. (2013b). On the balance of envelope and temporal fine structure in the encoding of speech in the early auditory system. *The Journal of the Acoustical Society of America*, *133*(5), 2818–33. doi:10.1121/1.4795783

Shannon, R., Zeng, F., & Kamath, V. (1995). Speech recognition with primarily temporal cues. *Science*. Retrieved from http://www.sciencemag.org/content/270/5234/303.short

Shannon, R. V., Zeng, F. G., Kamath, V., Wygonski, J., & Ekelid, M. (1995). Speech recognition with primarily temporal cues. *Science*, *270*(5234), 303-304.

Simon, H., & Yund, E. (1993). Frequency discrimination in listeners with sensorineural hearing loss. *Ear and hearing*. Retrieved from http://journals.lww.com/ear-hearing/Abstract/1993/06000/Frequency_Discrimination_in_Listeners_with.6.aspx

Small, S. A., & Stapells, D. R. (2005). Multiple auditory steady-state responses to bone-conduction stimuli in adults with normal hearing. *Journal of the American Academy of Audiology*, *16*(3), 172-183.

Smalt, C. J., Krishnan, A., Bidelman, G. M., Ananthakrishnan, S., & Gandour, J. T. (2012). Distortion products and their influence on representation of pitch-relevant information in the human brainstem for unresolved harmonic complex tones. *Hearing research*, *292*(1-2), 26–34. doi:10.1016/j.heares.2012.08.001

Smith, J. C., Marsh, J. T., & Brown, W. S. (1975). Far-field recorded frequency-following responses: evidence for the locus of brainstem sources.*Electroencephalography and clinical neurophysiology*, *39*(5), 465-472. Retrieved from http://www.sciencedirect.com/science/article/pii/0013469475900474

Smoorenburg, G. (1992). Speech reception in quiet and in noisy conditions by individuals with noise-induced hearing loss in relation to their tone audiogram. *The journal of the acoustical society of America*, 421–437. Retrieved from http://link.aip.org/link/?JASMAN/91/421/1

Smoski, W. J., & Trahiotis, C. (1986). Discrimination of interaural temporal disparities by normal-hearing listeners and listeners with high-frequency sensorineural hearing loss. *The Journal of the Acoustical Society of America*,*79*, 1541.

Snell, K. B., & Frisina, D. R. (2000). Relationships among age-related differences in gap detection and word recognition. *The Journal of the Acoustical Society of America*, *107*(3), 1615–26. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10738815

Snyder, R. L., Rebscher, S. J., Cao, K., Leake, P. A., & Kelly, K. (1990). Chronic intracochlear electrical stimulation in the neonatally deafened cat. I: Expansion of central representation. *Hearing research*, *50*(1), 7-33.

Snyder, R. L., & Schreiner, C. E. (1984). The auditory neurophonic: basic properties. *Hearing research*, *15*(3), 261–80. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/6501114

Song, J H, Banai, K., Russo, N. M., & Kraus, N. (2006). On the relationship between speech- and nonspeech-evoked auditory brainstem responses. *Audiology & neuro-otology*, *11*(4), 233–41. doi:10.1159/000093058

Song, J., Skoe, E., Wong, P., & Kraus, N. (2008). Song, J. H., Skoe, E., Wong, P. C., & Kraus, N. (2008). Plasticity in the adult human auditory brainstem following short-term linguistic training. *Journal of Cognitive Neuroscience*, *20*(10), 1892-1902. doi:10.1162/jocn.2008.20131.

Song, Judy H, Skoe, E., Banai, K., & Kraus, N. (2012). Training to improve hearing speech in noise: biological mechanisms. *Cerebral cortex (New York, N.Y. : 1991)*, *22*(5), 1180–90. doi:10.1093/cercor/bhr196

Souza, P. E., & Boike, K. T. (2006). Combining temporal-envelope cues across channels: effects of age and hearing loss. *Journal of speech, language, and hearing research : JSLHR*, *49*(1), 138–49. doi:10.1044/1092-4388(2006/011)

Starr, A., & Hellerstein, D. (1971). Distribution of frequency following responses in cat cochlear nucleus to sinusoidal acoustic signals. *Brain Research*, *33*(2), 367-377.

Stillman, R. D., Crow, G., & Moushegian, G. (1978). Components of the frequency-following potential in man. *Electroencephalography and Clinical Neurophysiology*, *44*(4), 438-446.

Stillman, R. D., Crow, G., & Moushegian, G. (1978). Components of the frequency-following potential in man. *Electroencephalography and Clinical Neurophysiology*, *44*(4), 438-446.

Strickland, E. A., & Viemeister, N. F. (1997). The effects of frequency region and bandwidth on the temporal modulation transfer function. *The Journal of the Acoustical Society of America*, *102*, 1799.

Summers, V., & Leek, M. (1998). F0 processing and the seperation of competing speech signals by listeners with normal hearing and with hearing loss. *Journal of Speech, Language and Hearing Research*. Retrieved from http://jslhr.asha.org/cgi/content/abstract/41/6/1294

Summers, V., & Leek, M. R. (1994). The internal representation of spectral contrast in hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *95*(6), 3518–28. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8046143

Swaminathan, J. (2010). *The role of envelope and temporal fine structure in the perception of noise degraded speech*. Retrieved from http://docs.lib.purdue.edu/dissertations/AAI3444758/

Swaminathan, J., Krishnan, A., & Gandour, J. T. (2008). Pitch encoding in speech and nonspeech contexts in the human auditory brainstem. *Neuroreport*, *19*(11), 1163–7. doi:10.1097/WNR.0b013e3283088d31

Syka, J. (2002a). Plastic changes in the central auditory system after hearing loss, restoration of function, and during learning. *Physiological Reviews*. Retrieved from http://physrev.physiology.org/content/82/3/601.short

Syka, J. (2002b). Plastic changes in the central auditory system after hearing loss, restoration of function, and during learning. *Physiological Reviews*. Retrieved from http://physrev.physiology.org/content/82/3/601.short

Ter Keurs, M., Festen, J. M., & Plomp, R. (1993). Effect of spectral envelope smearing on speech reception. II. *The Journal of the Acoustical Society of America*, *93*, 1547.

Thai-Van, H., Micheyl, C., Moore, B. C. J., & Collet, L. (2003). Enhanced frequency discrimination near the hearing loss cut-off: a consequence of central auditory plasticity induced by cochlear damage? *Brain : a journal of neurology*, *126*(Pt 10), 2235–45. doi:10.1093/brain/awg228

Takahashi, G. A., & Bacon, S. P. (1992). Modulation detection, modulation masking, and speech understanding in noise in the elderly. *Journal of Speech, Language and Hearing Research*, *35*(6), 1410.

Tucci, D., Merson, M., & Wilson, B. (2010). A summary of the literature on global hearing impairment: current status and priorities for action. *Otology & Neurotology*. Retrieved from http://journals.lww.com/otologyneurotology/Abstract/2010/01000/A_Summary_of_the_Literature_on_Global_Hearing.6.aspx

Tremblay, K. L., Piskosz, M., & Souza, P. (2002). Aging alters the neural representation of speech cues. *Neuroreport*, *13*(15), 1865–70. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12395081

Tremblay, K. L., Piskosz, M., & Souza, P. (2003). Effects of age and age-related hearing loss on the neural representation of speech cues. *Clinical Neurophysiology*, *114*(7), 1332–1343. doi:10.1016/S1388-2457(03)00114-7

Tucci, D., Merson, M., & Wilson, B. (2010). A summary of the literature on global hearing impairment: current status and priorities for action. *Otology & Neurotology*. Retrieved from http://journals.lww.com/otologyneurotology/Abstract/2010/01000/A_Summary_of_the_Literature_on_Global_Hearing.6.aspx

Turner, C. W., & Robb, M. P. (1987). Audibility and recognition of stop consonants in normal and hearing-impaired subjects. *The Journal of the Acoustical Society of America*, *81*, 1566.

Tyler, R. S., Summerfield, Q., Wood, E. J., & Fernandes, M. A. (1982). Psychoacoustic and phonetic temporal processing in normal and hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *72*, 740.

Tyler, R. S., Wood, E. J., & Fernandes, M. (1983). Frequency resolution and discrimination of constant and dynamic tones in normal and hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *74*(4), 1190–9. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/6643841

Veld, F. H. T., Osterhammel, P., & Terkildsen, K. (1977). The frequency selectivity of the 500 Hz frequency following response. *Scandinavian Audiology*,*6*(1), 35-42.

Vale, C., & Sanes, D. H. (2002). The effect of bilateral deafness on excitatory and inhibitory synaptic strength in the inferior colliculus. *European Journal of Neuroscience*, *16*(12), 2394–2404. doi:10.1046/j.1460-9568.2002.02302.x

Vihla, M., Lounasmaa, O. V, & Salmelin, R. (2000). Cortical processing of change detection: dissociation between natural vowels and two-frequency complex tones. *Proceedings of the National Academy of Sciences of the United States of America*, *97*(19), 10590–4. doi:10.1073/pnas.180317297

Villchur, E. (1973). Signal processing to improve speech intelligibility in perceptive deafness. *The Journal of the Acoustical Society of America*, *53*, 1646.

Villchur, E. (1974). Simulation of the effect of recruitment on loudness relationships in speech. *The Journal of the Acoustical Society of America*, *56*, 1601.

Vouloumanos, A., Kiehl, K. A., Werker, J. F., & Liddle, P. F. (2001). Detection of sounds in the auditory stream: event-related fMRI evidence for differential activation to speech and nonspeech. *Journal of Cognitive Neuroscience*, *13*(7), 994-1005. Retrieved from http://www.mitpressjournals.org/doi/abs/10.1162/089892901753165890

Wakefield, G. H., & Nelson, D. A. (1985). Extension of a temporal model of frequency discrimination: Intensity effects in normal and hearing-impaired listeners. *The Journal of the Acoustical Society of America*, *77*, 613.

Walton, J., Simon, H., & Frisina, R. (2002). Age-related alterations in the neural coding of envelope periodicities. *Journal of neurophysiology*, 565–578. Retrieved from http://jn.physiology.org/content/88/2/565.short

Wible, B., Nicol, T., & Kraus, N. (2004). Atypical brainstem representation of onset and formant structure of speech sounds in children with language-based learning problems. *Biological psychology*, *67*(3), 299–317. doi:10.1016/j.biopsycho.2004.02.002

Wible, B., Nicol, T., & Kraus, N. (2005). Correlation between brainstem and cortical auditory processes in normal and language-impaired children. *Brain : a journal of neurology*, *128*(Pt 2), 417–23. doi:10.1093/brain/awh367

Willott, J. (1996). Physiological plasticity in the auditory system and its possible relevance to hearing aid use, deprivation effects, and acclimatization. *Ear and Hearing*. Retrieved from http://journals.lww.com/ear-hearing/Abstract/1996/17031/Physiological_Plasticity_in_the_Auditory_System.7.aspx

Wojtczak, M. (1996). Perception of intensity and frequency modulation in people with normal and impaired hearing. *Psychoacoustics, Speech, and Hearing Aids*. *Singapore: World Scientific*, 35-38.

Wong, J., Miller, R., & Calhoun, B. (1998). Effects of high sound levels on responses to the vowel/ɛ/in cat auditory nerve. *Hearing research*, *123*, 61–77. Retrieved from http://www.sciencedirect.com/science/article/pii/S0378595598000987

Wong, P., Skoe, E., & Russo, N. (2007). Musical experience shapes human brainstem encoding of linguistic pitch patterns. *Nature neuroscience*. Retrieved from http://www.nature.com/neuro/journal/v10/n4/abs/nn1872.html

Woolf, N., Ryan, A., & Bone, R. (1981). Neural phase-locking properties in the absence of cochlear outer hair cells. *Hearing research*. Retrieved from http://www.sciencedirect.com/science/article/pii/0378595581900174

World Health Organization Deafness and Hearing loss (2013) http://who.int/mediacentre/factsheets/fs300/en/

Xu, L., & Pfingst, B. (2008). Spectral and temporal cues for speech recognition: implications for auditory prostheses. *Hearing research*, *242*, 132–140. doi:10.1016/j.heares.2007.12.010.Spectral

Xu, Y., Krishnan, A., & Jackson, T. (2006). Speci ¢ city of experience-dependent pitch representation in the brainstem, *17*(15), 1–5.

Yamada, O., Yamane, H., & Kodera, K. (1977). Simultaneous recordings of the brain stem response and the frequency-following response to low-frequency tone. *Electroencephalography and clinical neurophysiology*, *43*(3), 362-370. Retrieved from http://www.sciencedirect.com/science/article/pii/0013469477902590

Young, E. D., & Sachs, M. B. (1979). Representation of steady-state vowels in the temporal aspects of the discharge patterns of populations of auditory-nerve fibers. *The Journal of the Acoustical Society of America*, *66*(5), 1381–1403. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/500976

Zurek, P. M., & Formby, C. (1981). Frequency-discrimination ability of hearing-impaired listeners. *Journal of Speech, Language and Hearing Research*, *24*(1), 108.

APPENDIX

APPENDIX CASE HISTORY QUESTIONNAIRE

Name:
DOB:
Age:
Gender:

1. Have you ever had a hearing test before?
    a. Yes _____
        i. When? _____
    b. No _____

2. Do you have any difficulty hearing?
    a. Yes _____
        i. Which ear? Right _____ Left _____ Both _____
        ii. Better ear? Right _____ Left _____
    b. No _____

3. When did you first notice your hearing problem?

---

4. Is your hearing worse since you first noticed it, or since your last hearing test?
    a. Yes _____
    b. No _____

5. Was the onset of your hearing loss
    a. Gradual _____
    b. Sudden _____
    c. Fluctuating _____

6. What do you think caused your hearing loss?

_____

7. Have you ever had any ear-infections?
    a. Yes _____
        i. Which ear? Right _____ Left _____ Both _____

b. No _____

8. Have you ever had ear-surgery or tubes in your ears?
    a. Yes _____
        i. Which ear? Right _____ Left _____ Both _____
    b. No _____

9. Does anyone in your family have a hearing problem?
    a. Yes _____
        i. Who and what type? _____
    b. No _____
10. Do you hear noises in your ears or head?
    a. Yes _____
        i. Which ear? Right _____ Left _____ Both _____
    b. No _____

11. Check the following that best described the noises that you hear
    a. High pitched ringing
    b. Buzzing
    c. Roaring
    d. Pulsating
    e. Crickets
    f. Rushing water
    g. Other

12. How often do you hear the noises?
    a. Constantly
    b. Frequently
    c. Occasionally

13. Do you have any dizziness?
    a. Yes _____
        i. If yes, is it accompanied by:
            1. Nausea? Yes _____ No _____
    b. No _____

14. Do you ever find that sounds are too loud to tolerate?
    a. Yes _____
    b. No _____

15. Are you currently under a physician's care for any medical problems?
    a. Yes _____
    b. No _____

16. Check any illnesses that you have had:
    a. Meningitis
    b. Heart trouble
    c. Measles
    d. Mumps
    e. Chicken pox
    f. High blood pressure
    g. Malaria
    h. Head injuries
    i. Diabetes
    j. Scarlet fever
    k. Epilepsy
    l. Kidney problems
    m. Other

17. Do you take medications frequently?
    a. Yes _____
        i. If yes, please list type, quantity and duration:
           _____
    b. No _____

18. Have you ever been treated with Streptomycin, Neomycin, Kanamycin, Quinine, Cisplatin or Carboplatin?
    a. Yes _____
        i. If yes, please explain: _____
    b. No _____

19. Have you ever been exposed to loud noises for any length of time?
    a. Yes _____
        i. If yes, please describe: _____
    b. No _____

20. What is or was your occupation?

---

21. Have you had any kind of musical training?
    a. Yes _____
        i. If yes, please specify duration:
        ii. Type of training (instrument/vocal)
        iii. Type of instrument:
    b. No _____

22. Have you ever used a hearing aid?
    a. Yes _____
        i. If yes, please specify duration:

ii. Make and model of hearing aid:

b. No _____

23. Were/are you satisfied with your hearing aid?
    a. Yes _____
    b. No _____
        i. If no, specify reason: _____

24. Do you currently wear a hearing aid?
    a. Yes _____
    b. No _____

25. Are you interested in continuing hearing aid use
    a. Yes _____
    b. No _____

26. In what situations do you have difficulty hearing?
    a. Work
    b. T.V./Radio
    c. School
    d. Social activities
    e. Personal relationships
    f. Phone
    g. Direction of sound
    h. Theaters/movies
    i. Other

27. Which of the following situations would you say you have greater difficulty in?
    a. Quiet situations
    b. Noisy situations
    c. Both are affected equally

VITA

VITA

Saradha Ananthakrishnan
Department of Speech, Language & Hearing Sciences, Purdue University

Education

B.Sc., (Hearing, Language & Speech), 2004, Maharashtra University of Health Sciences, India
Au.D., 2012 Purdue University, West Lafayette, Indiana
Ph.D., (Hearing Science), 2013, Purdue University, West Lafayette, Indiana

Professional Experience

Assistant Professor August 2013—present
Dept. of Audiology, Speech Language Pathology & Deaf Studies, Towson University

Research Interests

- Characterize the human frequency following response to steady state vowels, time varying diphthongs and speech in background noise in normal hearing and sensorineural hearing impairment.
- Statistical modeling of various demographic, behavioral and electrophysiological factors and sensorineural hearing loss.
- Neural plasticity in the auditory system
- Cortical potentials in normal hearing and hearing impaired populations; relationship between cortical and subcortical evoked potentials.

Publications, Abstracts, Conference Proceedings & Presentations:

Publications:

- Krishnan, A., Bidelman, G. M., Smalt, C. J., Ananthakrishnan, S., & Gandour, J. T. (2012). Relationship between brainstem, cortical and behavioral measures relevant to pitch salience in humans. *Neuropsychologia* 50, 2849-2859.

- Smalt, C. J., Krishnan, A., Bidelman, G. M., Ananthakrishnan, S., & Gandour, J. T. (2012). Distortion products and their influence on representation of pitch-relevant information in the human brainstem for unresolved harmonic complex tones. *Hearing Research 292*, 26-34.

- Krishnan, A., Gandour, J. T., Ananthakrishnan, S., Bidelman, G. M., & Smalt, C. J. (2011). Functional ear (a) symmetry in brainstem neural activity relevant to encoding of voice pitch: A precursor for hemispheric specialization? *Brain and language*, *119*(3), 226-231.

- Krishnan, A., Gandour, J. T., Ananthakrishnan, S., Bidelman, G. M., & Smalt, C. J. (2011). Linguistic status of timbre influences pitch encoding in the brainstem. *NeuroReport*, *22*(16), 801.

Poster presentations:

- Ananthakrishnan, S., Krishnan, A. (2012). Sub-cortical pitch encoding of speech sounds in the normal and impaired auditory systems. Poster to be presented at the *36th Meeting of the Association for Research in Otolaryngology (ARO)*, Baltimore, MD, February 16-20, 2013.

- Ananthakrishnan, S., Krishnan, A., Smalt, C.J., Bidelman, G.M. (2012). Brainstem neural encoding of envelope and temporal fine structure of complex stimuli in normal and impaired ears. Poster presented at the *35th Meeting of the Association for Research in Otolaryngology (ARO)*, San Diego, California, February 25-29, 2012.

- Krishnan, A., Smalt, C.J., Bidelman, G.M., Ananthakrishnan, S., Gandour, J.T. (2012). Concurrent neural representations in auditory brainstem and cortex predict the perceptual salience of pitch. Poster presented at the *35th Meeting of the Association for Research in Otolaryngology (ARO)*, San Diego, California, February 25-29, 2012

- Ananthakrishnan, S., Krishnan, A., Gandour, J.T., Bidelman, G.M., Smalt, C.J. (2011). Brainstem Origins of the Differential Hemispheric Laterality for Linguistic and Non Linguistic Pitch. Poster presented at
  - *34th Meeting of the Association for Research in Otolaryngology (ARO)*, Baltimore, M.D., February 19-23, 2011
  - *74th Annual Spring Convention of the Indiana Speech Language and Hearing Association (ISHA)*, Indianapolis, IN, March 30-April 2, 2011.

- Ananthakrishnan, S., Krishnan, A., Bidelman, G.M. (2010). Human Frequency Following Response: Differential Responses to Positive and Negative Iterated Rippled Noise (IRN) Stimuli.
  - Poster presented at the *33rd Meeting of the Association for Research in Otolaryngology (ARO)*, Anaheim, California, February 6-10, 2010.
  - Talk presented at Purdue University, Robert L. Ringel Symposium, April 30, 2010.

Awards, Funding & Honors

Graduate Level:

- Travel Award for Audiologists (*ARO*) (December 2011)
- SLHS Friends and Alumni Scholarship (*Purdue University)* (March 2011)
- Outstanding Student Clinician Award for 2011 (*ISHA)* (March 2011)
- Wilson Travel Scholarship *(Purdue University)* (January 2010)
- Weinberg Funds for research *(Purdue University)* (May 2009)
- Ross Fellowship *(Purdue University)* (August 2008)

Undergraduate Level:

- J.N. Tata Endowment Scholarship *(Sir Dorabji Tata Trust)* (August 2008)
- University First *(Maharashtra University of Health Sciences)* (2004-07)
- Gold Medalist *(Maharashtra University of Health Sciences)* (2004-07)
- J.R.D. Tata Scholarship *(Sir Dorabji Tata Trust)* (2004-07)
- Diplôme de la Langue Française *(Alliance Française de Bombay)* (2004)

Computer Skills: Data acquisition systems (Intelligent Hearing Systems, Bio-logic, Advanced Neuro Technology), Praat, Statistical Analysis Software (SAS), MATLAB, MS Office

Graduate School Work Experience

Research Assistantship:

Auditory Electrophysiology Laboratory (Summer 2009-
PI: Ravi Krishnan, Ph.D.

Instructor

Auditory Evoked Potentials (Spring 2013)
Graduate level course where responsibilities included preparation of teaching material, lecturing, conducting laboratory sessions and grading

Teaching Assistantship:

- Acoustic Bases for Speech and Hearing Sciences (Spring 2011)
  Instructor: Alexander Francis, Ph.D.
- Introduction to Assessment Audiology (Fall 2010)
  Instructor: Lata Krishnan, Ph.D.

Clinical Training

- Diagnostic audiology
  - Adult, infant, and pediatric hearing assessments
  - Vestibular testing & annual industrial hearing testing of employees
  - Preschool speech, language and hearing screenings
  - Exposure to various ear related pathologies
- Amplification

  - Hearing aid evaluation, selection, fitting, verification and troubleshooting
  - Earmold impressions
- Cochlear Implants
  - Device selection, programming, fitting & troubleshooting
  - Candidacy testing & Orientation
- Adult and pediatric aural rehabilitation
- Adult and pediatric speech, language & voice assessment and therapy, at undergraduate level
- Pediatric psychological evaluations, at undergraduate level

Clinical Audiology Externships:

- Indiana University Medical Center, IN. (Summer 2011-Summer 2012)
- IU Health Arnett, Lafayette, IN. (Spring 2011)
- Otolaryngology Associates, Indianapolis, IN. (Fall 2010)

Audiology Graduate Clinician:

- Indiana Veterans' Home, West Lafayette, IN. (Summer 2010)
- MD Steer Audiology Clinic (Fall 2008- Fall 2010)
  Purdue University, West Lafayette, IN.

Undergraduate Level:

- The Research Society for the Care, Treatment & Training of Children In Need of Special Care, Sewri, Mumbai, India. (Summer 2008)
- Lokmanya Tilak Municipal Medical College. (Spring 2008)
  Mumbai, India
- Rochiram Thadani Special School for Hearing Impaired. (Winter 2007)
  Mumbai, India
- Wadia Children's Hospital (Fall 2007)
  Mumbai, India
- Ali Yavar Jung National Institute for the Hearing Handicapped. (2004-2008)
  Mumbai, India

Professional Organization Membership

Association for Research in Otolaryngology (October 2009-